



United States Department of Agriculture

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# **Beverage Consumption and Growth, Size, Body Composition, and Risk of Overweight and Obesity: A Systematic Review**

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2020 Dietary Guidelines Advisory Committee,  
Beverage and Added Sugars Subcommittee

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Nutrition Evidence Systematic Review  
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This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee in collaboration with the Nutrition Evidence Systematic Review (NESR) team at the Center for Nutrition Policy and Promotion, Food and Nutrition Service, U.S. Department of Agriculture (USDA). All systematic reviews from the 2020 Advisory Committee Project are available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews>.

Conclusion statements drawn as part of this systematic review describe the state of science related to the specific question examined. Conclusion statements do not draw implications, and should not be interpreted as dietary guidance. This portfolio provides the complete documentation for this systematic review. A summary of this review is included in the 2020 Advisory Committee's Scientific Report available at [www.DietaryGuidelines.gov](http://www.DietaryGuidelines.gov).

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USDA and HHS implemented a process to identify topics and scientific questions to be examined by the 2020 Dietary Guidelines Advisory Committee. The Committee conducted its review of evidence in subcommittees for discussion by the full

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<sup>i</sup> Under contract with the Food and Nutrition Service, United States Department of Agriculture.

Committee during its public meetings. The role of the Committee members involved establishing all aspects of the protocol, which presented the plan for how they would examine the scientific evidence, including the inclusion and exclusion criteria; reviewing all studies that met the criteria they set; deliberating on the body of evidence for each question; and writing and grading the conclusion statements to be included in the scientific report the 2020 Committee submitted to USDA and HHS. The NESR team with assistance from Federal Liaisons and Project Leadership, supported the Committee by facilitating, executing, and documenting the work necessary to ensure the reviews were completed in accordance with NESR methodology. More information about the 2020 Dietary Guidelines Advisory Committee, including the process used to identify topics and questions, can be found at [www.DietaryGuidelines.gov](http://www.DietaryGuidelines.gov). More information about NESR can be found at [NESR.usda.gov](http://NESR.usda.gov).

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## INTRODUCTION

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This document describes a systematic review conducted to answer the following question: What is the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity? This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee, supported by USDA's Nutrition Evidence Systematic Review (NESR).

More information about the 2020 Dietary Guidelines Advisory Committee is available at the following website: [www.DietaryGuidelines.gov](http://www.DietaryGuidelines.gov).

NESR specializes in conducting food- and nutrition-related systematic reviews using a rigorous, protocol-driven methodology. More information about NESR is available at the following website: [NESR.usda.gov](http://NESR.usda.gov).

NESR's systematic review methodology involves developing a protocol, searching for and selecting studies, extracting data from and assessing the risk of bias of each included study, synthesizing the evidence, developing conclusion statements, grading the evidence underlying the conclusion statements, and recommending future research. A detailed description of the systematic reviews conducted for the 2020 Dietary Guidelines Advisory Committee, including information about methodology, is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews>. In addition, starting on page 328, this document describes the final protocol as it was applied in the systematic review. A description of and rationale for modifications made to the protocol are described in the 2020 Dietary Guidelines Advisory Committee Report, Part D: Chapter 10. Beverages.

## List of abbreviations

Abbreviation	Full name
BMI	Body mass index
CNPP	Center for Nutrition Policy and Promotion
FNS	Food and Nutrition Service
HDI	Human development index
HHS	Health and Human Services
LNCSB	Low or no calorie sweetened beverage
NESR	Nutrition Evidence Systematic Review
NRCT	Non-randomized controlled trials
OASH	Office of the Assistant Secretary for Health
ODPHP	Office of Disease Prevention and Health Promotion
ONGA	Office of Nutrition Guidance and Analysis
PICO	Population, intervention/exposure, comparators, and outcomes
PCS	Prospective cohort study
RCT	Randomized controlled trials
SSB	Sugar-sweetened beverage
UK	United Kingdom
US	United States
USDA	U.S. Departments of Agriculture

# WHAT IS THE RELATIONSHIP BETWEEN BEVERAGE CONSUMPTION AND GROWTH, SIZE, BODY COMPOSITION, AND RISK OF OVERWEIGHT AND OBESITY?

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## PLAIN LANGUAGE SUMMARY

### What is the question?

- The question is: What is the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity?

### What is the answer to the question?

- Milk:
  - Limited evidence suggests that milk intake is not associated with adiposity in children.
  - Insufficient evidence is available to draw a conclusion about the relationship between the type of milk (i.e., milk fat content, flavor) and adiposity in children.
  - Limited evidence suggests that higher milk intake is associated with a greater increase in height compared to lower intake in children.
  - Limited evidence suggests that milk intake is not associated with adiposity in adults.
- 100% Juice:
  - Limited evidence suggests 100% juice intake in children is not associated with adiposity or height in children.
  - Limited evidence suggests 100% juice consumption is not associated with measures of adiposity in adults.
- Sugar-sweetened beverages:
  - Moderate evidence suggests that higher sugar-sweetened beverage intake is associated with greater adiposity in children.
  - Limited evidence suggests that higher sugar-sweetened beverage intake is associated with greater adiposity in adults.
  - Insufficient evidence is available to determine the relationship between sugar-sweetened beverages compared with low- and no- calorie sweetened beverages on adiposity in children.
  - Limited evidence suggests no association between sugar-sweetened beverages compared with low- and no- calorie sweetened beverages on adiposity in adults.
- Low and no-calorie sweetened beverages:
  - Limited evidence suggests no association between low- and no-calorie sweetened beverage consumption and adiposity in children.
  - Limited evidence suggests that low- and no- calorie sweetened beverage consumption is associated with reduced adiposity in adults.

### Why was this question asked?

- This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.

### **How was this question answered?**

- The 2020 Dietary Guidelines Advisory Committee, Beverage and Added Sugars Subcommittee conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.

### **What is the population of interest?**

- Healthy people and/or those at risk for chronic disease, ages 2 and older were included in this evidence.

### **What evidence was found?**

- This review includes 152 articles that examined drinking milk (62 articles), 100% juice (42 articles), sugar-sweetened beverages (SSBs, 76 articles), or low- and no-calorie sweetened beverages (LNCSBs, 37 articles). Some articles examined more than one type of beverage.
- Most studies examined outcomes related to adiposity. Examples of these outcomes are: BMI, BMI above a cutoff (i.e., overweight, obesity), waist circumference, and body fat.
- Milk: Few studies reported significant associations, which suggests that the amount of milk children and adults drink is not associated with adiposity. However, children who drank more milk tended to grow taller than children who drank less milk. The articles did not provide enough evidence to draw conclusions about the type of milk children drink (i.e., milk fat levels, flavored milk) and adiposity.
- 100% Juice: Evidence from the highest-quality studies suggests that the amount of 100% juice children and adults drink is not associated with adiposity.
- SSBs: Most studies compared drinking SSBs with drinking less SSBs or drinking water instead of drinking SSBs. These studies tended to find that children and adults who drink SSBs have higher adiposity than children and adults who drink less SSBs or drink water instead. A small number of studies compared drinking SSBs with drinking LNCSBs. This evidence tended to be inconsistent. In children, there was not enough evidence to draw a conclusion about drinking SSBs compared with LNCSBs and adiposity. In adults, the evidence suggested that there is no association.
- LNCSBs: Few studies in children reported significant associations, which suggests that the amount of LNCSBs children drink is not associated with adiposity. In contrast, most studies in adults (including the highest-quality studies) reported that adults who drink more LNCSBs have lower adiposity than adults who drink less.
- The evidence has several limitations. The studies differed from one another in some important ways, such as the outcomes that were measured and the way the beverage exposure was defined. Some studies may not have been long enough or may not have studied enough participants to detect associations. Factors other than beverage consumption may impact the outcomes, and these factors were not always carefully addressed in the studies' analyses.

### **How up-to-date is this systematic review?**

This review searched for studies from January 2000 to June 2019, with the exception of evidence on sugar-sweetened beverage consumption compared to a different amount of sugar-sweetened beverage consumption or water, in which the search included studies from January 2012 to June 2019.

# TECHNICAL ABSTRACT

## Background

- This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.
- The 2020 Dietary Guidelines Advisory Committee, Beverage and Added Sugars Subcommittee conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.
- The goal of this systematic review was to examine the following question: What is the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity?

## Conclusion statements and grades

- **Milk:**
  - Limited evidence suggests that milk intake is not associated with adiposity in children. (Grade: Limited)
  - Insufficient evidence is available to draw a conclusion about the relationship between the type of milk (i.e., milk fat content, flavor) and adiposity in children. (Grade: Grade not assignable)
  - Limited evidence suggests that higher milk intake is associated with a greater increase in height compared to lower intake in children. (Grade: Limited)
  - Limited evidence suggests that milk intake is not associated with adiposity in adults. (Grade: Limited)
- **100% Juice:**
  - Limited evidence suggests 100% juice intake in children is not associated with adiposity or height in children. (Grade: Limited)
  - Limited evidence suggests 100% juice consumption is not associated with measures of adiposity in adults. (Grade: Limited)
- **Sugar-sweetened beverages:**
  - Moderate evidence suggests that higher sugar-sweetened beverage intake is associated with greater adiposity in children. (Grade: Moderate)
  - Limited evidence suggests that higher sugar-sweetened beverage intake is associated with greater adiposity in adults. (Grade: Limited)
  - Insufficient evidence is available to determine the relationship between sugar-sweetened beverages compared with low- and no- calorie sweetened beverages on adiposity in children. (Grade: Grade not assignable)
  - Limited evidence suggests no association between sugar-sweetened beverages compared with low- and no- calorie sweetened beverages on adiposity in adults. (Grade: Limited)
- **Low and no-calorie sweetened beverages:**
  - Limited evidence suggests no association between low- and no-calorie sweetened beverage consumption and adiposity in children. (Grade: Limited)
  - Limited evidence suggests that low- and no- calorie sweetened beverage consumption is associated with reduced adiposity in adults. (Grade: Limited)

## Methods

- A literature search was conducted using 3 databases (PubMed, Cochrane, Embase) to identify articles that evaluated the intervention or exposure of non-alcoholic beverage consumption and the outcomes of growth, size, body composition, and risk of overweight and obesity. A manual search was conducted to identify articles that may not have been included in the electronic databases searched. Articles were screened by two NESR analysts independently for inclusion based on pre-determined criteria.
- Data extraction and risk of bias assessment were conducted for each included study, and both were checked for accuracy. The Committee qualitatively synthesized the body of evidence to inform development of a conclusion statement(s), and graded the strength of evidence using pre-established criteria for risk of bias, consistency, directness, precision, and generalizability.

## Summary of the evidence

### Milk:

- The body of evidence includes 62 papers: 30 papers on children and 32 papers on adults. Of the evidence on children, there were 4 papers from randomized controlled trials (RCTs) and 26 papers from longitudinal cohort studies. Of the evidence on adults, there were 7 papers from RCTs; 24 papers from prospective cohort studies; and 1 paper using a Mendelian Randomization design.
- To discern healthy growth from excessive growth in children, weight status (i.e., prevalence or incidence of overweight or obesity), BMI and BMI z-scores, and body composition measures (e.g., waist circumference and body fat), were considered to reflect “adiposity.”
  - The majority of the findings for these outcomes were not significant. The few findings that were significant were not consistent in direction.
- To assess healthy growth in children, outcomes such as height and lean mass were considered. Four studies reported height as an outcome: 3 cohort studies reported a significant positive association between milk intake and height in children, and 1 RCT found no effect of milk intake on height compared to drinking water though this study’s duration was only 12 weeks.
- Seven cohort studies specifically examined types of milk (i.e. milk fat levels, flavored milk) and adiposity outcomes in children; however, the results were not consistent.
- The majority of the studies in adults found no significant association between milk intake and adiposity; there were some significant associations; however, these were inconsistent in direction.
- The body of evidence from children and adults has several significant limitations including lack of specificity and consistency in definition of the exposure, the use of non-validated methods for assessing beverage intake, uncontrolled confounding, and inconsistencies in findings. More research is needed to address these issues.

### **100% Juice:**

- 42 papers examining the relationship between 100% juice intake and outcomes related to growth, size, body composition, and risk of overweight or obesity were included in this body of evidence.
- Studies published between January 2000 and June 2019 were synthesized by age group
  - Children: 23 studies, including 1 RCT and 22 prospective cohort studies
  - Adults: 19 studies, including 4 RCTs, 1 NRCT, and 14 prospective cohort studies
- Evidence in children
  - The 1 RCT and the majority of the higher quality prospective cohort studies found no statistically significant relationship between 100% juice intake and adiposity.
  - The few studies that were significant were not consistent in direction.
  - The evidence in children was limited by lack of clarity in defining the juice exposure; inconsistent quantification of juice consumption, inconsistent measures of adiposity, lack of evidence from stronger study designs, and inadequate adjustment for confounders.
- Evidence in adults
  - The 4 RCTs and 1 NRCT found no statistically significant relationship between 100% juice intake and adiposity.
  - The prospective cohort studies found inconsistent evidence depending on the specific measure of adiposity. For example, roughly half of the studies (n=4) found that greater consumption of 100% juice intake was related to a greater increase in weight, while the others (n=3) found no significant relationship. Studies examining waist circumference were more consistent, with 5 of the 6 studies finding no significant association with 100% juice intake. Further, all studies (n=3) examining body fat or prevalence of (abdominal) obesity found no significant associations with 100% juice intake.
  - The evidence from the RCTs and NRCT were limited by the short durations small sample sizes.
  - The evidence from the prospect cohort studies were limited by the single measurement of the exposure, reliance on self-reported outcome data, inadequate adjustment for confounders, and limited generalizability of the experimental data.

### **Sugar-sweetened beverages:**

- 76 studies identified via a literature search from June 2012 to June 2019 were included in this systematic review. Studies were synthesized based on comparator (no/different amount of sugar-sweetened beverage or low/no-calorie sweetened beverage) and age of participants (children or adults).
  - Sugar-sweetened beverage (SSB) consumption compared to different amounts or water
    - Children: 46 articles

- RCTs: 2 articles
  - NRCTs: 1 article
  - Prospective cohort studies: 43 articles
- Adults: 27 articles
  - RCTs: 3 articles
  - NRCTs: 1 article
  - Prospective cohort studies: 23 articles
- Sugar-sweetened beverage consumption compared to low- or no-calorie sweetened beverages (LNCSB)
  - Children: 2 articles
    - RCTs: 2 articles
  - Adults: 6 articles
    - RCTs: 5 articles
    - Prospective cohort studies: 1 article
- In studies examining SSB intake in children, the majority of studies (~80%) reported a significant effect or association between SSB intake and adiposity, however this was not always consistent within studies that reported multiple outcome measures. There were additional concerns related to risk of bias and generalizability.
- In studies examining SSB intake in adults, the majority of studies (~70%) reported a significant effect or association between SSB intake and adiposity; however, this was not always consistent within studies that reported multiple outcome measures. The 3 included RCTs had significant risk of bias concerns related to the methodology, particularly around the comparator, and concerns with generalizability.
- Two articles from one RCT addressed the relationship between SSB compared to LNCSB intake in children and there was insufficient evidence to draw a conclusion.
- In studies comparing intake of SSBs and LNCSB in adults, there was inconsistency in findings and in methodology. Of the 5 RCTs, 3 did not find a significant difference between groups, however 2 of these studies had small sample sizes and may have been underpowered. Of the 2 studies that did report a significant effect, there was not a significant effect across all reported outcomes. For example, one study reported differences based on the type of sweetener within LNCSB and the other did not find a difference in weight or BMI between groups, but did report that those who consumed LNCSB were more likely to achieve 5% weight loss.

#### **Low and no-calorie sweetened beverages:**

- There were 37 studies identified via literature search from January 2000 to June 2019 included in this systematic review that examined the relationship between LNCSB and outcomes related to growth, size, body composition, and risk of overweight and obesity.
  - Of the 17 papers in children, all were prospective cohort studies.
  - Of the 20 papers in adults, 6 were from RCTs and 14 were from prospective cohort studies.
- In studies examining LNCSB intake in children, the majority of studies (~75%) reported no association for the main outcome measure(s) of adiposity among the



study populations. The remaining studies had mixed associations and methodologic concerns.

- 3 papers with findings of increased adiposity measures
  - 1 paper with findings of decreased adiposity measures<sup>1</sup>
  - 1 paper only reported height-related outcomes<sup>2</sup>
- The body of evidence from children had several limitations
  - Inadequate adjustment for confounders
  - Inconsistency in methods for assessing beverage intake
  - Short study duration
  - High attrition
- In studies examining LNCSB intake in adults, the majority of studies (72%) reported a significant effect or association between LNCSB intake and adiposity; however, this was not always consistent within studies that reported multiple outcome measures.
  - One well-designed RCT and two large prospective cohort studies reported an association between LNCSB and reduced adiposity.
- The body of evidence from adults had several limitations
  - Experimental studies: short study duration, no assessment of compliance, and difference in comparators
  - Cohort studies: confounding, difference in assessment methods, poor generalizability, and high attrition

## **FULL REVIEW**

### **BEVERAGE: MILK**

What is the relationship between beverage consumption (milk) and growth, size, body composition, and risk of overweight and obesity?

#### **Conclusion statements and grades**

Limited evidence suggests that milk intake is not associated with adiposity in children. (Grade: Limited)

Insufficient evidence is available to draw a conclusion about the relationship between the type of milk (i.e., milk fat content, flavor) and adiposity in children. (Grade: Grade not assignable)

Limited evidence suggests that higher milk intake is associated with a greater increase in height compared to lower intake in children. (Grade: Limited)

Limited evidence suggests that milk intake is not associated with adiposity in adults. (Grade: Limited)

#### **Summary of the evidence**

- The body of evidence includes 62 articles: 30 articles on children and 32 articles on adults.<sup>1-62</sup> Of the evidence on children, there were 4 papers from randomized controlled trials (RCTs) and 26 papers from longitudinal cohort studies. Of the evidence on adults, there were 7 papers from RCTs; 24 papers from prospective cohort studies; and 1 paper using a Mendelian Randomization design.
- To discern healthy growth from excessive growth in children, weight status (i.e., prevalence or incidence of overweight or obesity), BMI and BMI z-scores, and body composition measures (e.g., waist circumference and body fat), were considered to reflect “adiposity”.
  - The majority of the findings for these outcomes were not significant. The few findings that were significant were not consistent in direction.
- To assess healthy growth in children, outcomes such as height and lean mass were considered. Four studies reported height as an outcome: 3 cohort studies reported a significant positive association between milk intake and height in children, and 1 RCT found no effect of milk intake on height compared to drinking water though this study’s duration was only 12 weeks.
- Seven cohort studies specifically examined types of milk (i.e. milk fat levels, flavored milk) and adiposity outcomes in children; however, the results were not consistent.
- The majority of the studies in adults found no significant association between milk intake and adiposity; there were some significant associations; however, these were inconsistent in direction.
- The body of evidence from children and adults has several significant limitations

including lack of specificity and consistency in definition of the exposure, the use of non-validated methods for assessing beverage intake, uncontrolled confounding, and inconsistencies in findings. More research is needed to address these issues.

## Description of the evidence

Of the 152 included articles in this systematic review on the relationship between non-alcoholic beverage consumption and outcomes related to growth, size, body composition, and risk of overweight and obesity, there were 62 articles in the body of evidence related to milk consumption (30 articles in children, 32 articles in adults). Specifically for the systematic review of milk consumption and growth, size, body composition, and risk of overweight and obesity, the exposure or intervention was milk, which included dairy milk and milk substitutes. This could include a composition of different types of milk, such as different levels of milk fat (e.g., skim milk, reduced fat, and whole milk), flavored milk, etc. Dairy milk was the exposure or intervention beverage in all studies within the body of evidence; no studies using milk substitutes met the inclusion criteria. The comparator was defined as a different amount (including no intake) of the same beverage type, water, or milk with different fat levels (e.g., skim milk versus whole milk). The search range included peer-reviewed articles published from January 2000 to June 2019. Studies were included if they were conducted in countries categorized as high or very high on the Human Development Index<sup>ii</sup> and with generally healthy participants or those at risk for chronic disease, aged 2 years and older. Studies with the following designs were included: RCTs, non-randomized controlled trials (NRCTs), prospective and retrospective cohort studies, nested case-control studies, and Mendelian Randomization. The studies in children and in adults were reviewed and synthesized independently.

### *Study designs:*

- Children: 30 articles (**Table 1**)
  - RCTs: 4 articles
  - Prospective cohort studies: 26 articles
- Adults: 32 articles (**Table 4**)
  - RCTs: 7 articles
  - Prospective cohort studies: 24 articles
  - Mendelian randomization: 1 article

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<sup>ii</sup> The Human Development classification was based on the Human Development Index (HDI) ranking (1) from the year the study intervention occurred or data was collected. If the study did not report the year in which the intervention occurred or data was collected, the HDI classification for the year of publication was applied. HDI values are available from 1980, and then from 1990 to present. If a study was conducted in 2018 or 2019, the most current HDI classification was applied. If a study was conducted prior to 1990, the HDI classification from 1990 was applied. When a country was not included in the HDI ranking, the current country classification from the World Bank (2) is used instead; 1. UN Development Program. HDI 1990-2017 HDRO calculations based on data from UNDESA (2017a), UNESCO Institute for Statistics (2018), United Nations Statistics Division (2018b), World Bank (2018b), Barro and Lee (2016) and IMF (2018). Available from: <http://hdr.undp.org/en/data>; 2. The World Bank. World Bank country and lending groups. Available from: <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-country-and-lending-groups>

## **Milk: Children**

### ***Population***

This body of evidence in children included 30 articles, with a baseline age ranging from 2 to 14 years. Across all studies, the majority were from the United States; however, several other high or very high HDI countries were represented, including: Australia, Canada, Denmark, Hong Kong, Portugal, and the UK. The analytic sample sizes ranged from 49 to 13,514. The predominant race/ethnic group represented in this evidence was non-Hispanic white; however, there were 6 studies where more than half of participants at baseline were not non-Hispanic white.<sup>14,26,34,39,51,55</sup>

### ***Intervention/exposure and comparator***

There were 2 RCTs that yielded 4 articles in this evidence base. In the RCT reported on by Arnberg et al,<sup>3</sup> Larnkjaer et al,<sup>35</sup> and Larnkjaer et al,<sup>36</sup> overweight adolescents were randomized to drink 1 L/day of 1 of 4 intervention drinks (water, skim milk, whey, or casein) for 12 weeks. The RCT by Lambourne et al<sup>34</sup> randomized adolescents to drink either milk, water, or juice throughout a 6-month resistance-training program. For both studies (4 papers), the intervention groups that were assigned to drink milk or water were included in this review, in accordance with the inclusion criteria.

Within the 26 papers from cohort studies, all but 3 papers<sup>15,45,59</sup> included either a continuous or categorical measure of milk intake as the exposure, with milk intake representing a combination of different types of milk and sometimes including flavored milk. Sixteen papers included plain and flavored milk in the exposure.<sup>1,2,6-</sup>

<sup>8,11,14,21,26,27,33,41,44,45,55,62</sup> Seven studies included an analysis of exposures based on type of milk, most often fat content,<sup>14,15,17,29,51,59</sup> although one study defined the exposure solely as flavored milk intake.<sup>45</sup> Follow-up times varied from about 6 months to about 15 years.

### ***Outcomes***

To discern 'healthy growth' from 'excessive growth' in children, weight status (prevalence or incidence of overweight or obesity), BMI and BMI z-scores, and body composition measures such as waist circumference and body fat, were considered to reflect "adiposity". To assess 'healthy growth' in children, outcomes such as height and lean mass were considered.

In children, BMI-related outcomes, including BMI, BMI z-score and incidence of overweight or obesity were the most commonly reported outcomes. Fewer papers (n=8) reported body composition measures (e.g., body fat percentage, fat-free mass, waist circumference). Six papers reported height as an outcome; 3 of these papers reported height as the only health-related outcome,<sup>2,6,35</sup> although other weight-related outcomes from these studies were reported in other publications included in this body of evidence.

### ***Evidence synthesis***

Four articles from two RCTs reported on outcomes related to adiposity.<sup>3,34-36</sup> An intervention in Denmark found that overweight adolescents randomized to drink 1 L/day of skim milk for 12 weeks resulted in higher weight, BMI, and change in BMI-for-

age z-scores compared to those randomized to drink 1 L/day of water.<sup>3,35,36</sup> This was likely due to a decrease in energy intake in the group that drank water rather than an effect of drinking milk. Participants assigned to the water group consumed fewer calories/d after compared to before the intervention; meanwhile, participants assigned to the milk intervention had no change in energy intake after compared to before the intervention. The second RCT, which included resistance training as part of the 6-month intervention, found no significant differences in BMI or body composition measures, including waist circumference, fat mass, and fat-free mass, between adolescents randomized to consume water or a combination of fat-free chocolate milk and 1%-fat white milk.<sup>34</sup> The results from the two RCTs do not support a relationship between milk intake and adiposity outcomes in adolescents.

Among cohort studies, 4 reported on the incidence or prevalence of overweight or obesity. Three studies found no significant association between milk intake and prevalence or incidence of overweight or obesity.<sup>8,14,29</sup> One study found that, in adolescent boys, greater baseline milk intake and greater increases in milk intake at the 5-year follow-up were associated with lower odds of incident overweight<sup>26</sup>; however, this study reported no significant association between milk intake and prevalence of overweight in boys, and, in girls, no association between milk intake and prevalence or incidence of overweight.

Fifteen cohort studies reported no significant association between milk intake and BMI or BMI z-scores.<sup>1,7,8,11,14,27,29,33,37,39-41,43,55,62</sup> A study in monozygotic twins found a correlation between intrapair differences in intake at age 9 and intrapair differences in BMI change from age 9-14 for the full sample of boys and girls and for girls alone, such that greater milk intake was associated with greater increases in BMI. Results were similar when looking specifically at low-fat milk intake, but there was no association in boys or for high fat milk.<sup>17</sup>

Of the 4 cohort studies that reported on body fat,<sup>1,21,26,44</sup> 1 found a significant association between increased milk intake and decreased body fat<sup>26</sup>; however, there was no association between milk intake and waist circumference. One additional study reported on waist circumference, finding that an increase in milk intake from ages 3 to 5 was associated with a smaller change in waist circumference from ages 5 to 6 compared to change in waist circumference in children who drank less milk.<sup>33</sup>

A subset of studies (n=7) looked at the association of milk intake, based on fat content of the milk, and adiposity in children.<sup>14,15,17,29,44,51,59</sup> Findings were inconsistent. Most studies reported a mix of significant and non-significant findings; and across the studies, the findings that were significant were not consistent in direction.

Across adiposity-related outcomes for both RCTs and prospective cohort studies, the evidence does not support an association between milk intake and adiposity in children. Insufficient evidence is available to draw conclusions related to milk type.

Regarding height, 3 cohort studies and 1 RCT reported results related to milk intake. Each of the cohort studies reported an association between higher milk intake and increased height in children.<sup>2,6,14</sup> The RCT did not find a significant effect of drinking milk compared to drinking water; however, this may be limited by the short duration of 12 weeks.<sup>35</sup> While more studies are needed, this evidence supports a potential association between milk intake and height in children.

Energy intake is an important covariate when interpreting studies on the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity because beverages might displace nutrient-dense foods or add additional energy to the diet. Therefore, findings with and without adjustments for energy intake were extracted and reviewed. Conclusion statements reflect the totality and strength of the evidence considering both approaches. Also, funding sources were documented during data extraction for consideration when reviewing this evidence. Further, publication bias is always a consideration in systematic reviews. This body of evidence includes both large and small studies and includes several studies that only report non-significant findings, therefore publication bias is not a serious concern.

### **Assessment of the evidence<sup>iii</sup>**

The conclusion statement “evidence suggests that milk intake is not associated with adiposity in *children*” was assigned a grade of **limited**. The conclusion statement “evidence suggests that higher milk intake is associated with a greater increase in height compared to lower intake in *children*” was assigned a grade of **limited**. There was insufficient evidence to draw a conclusion about the relationship between the type of milk (i.e., milk fat content, flavor) and adiposity in *children*. As outlined and described below, the body of evidence examining milk consumption and growth, size, body composition, and risk of overweight and obesity in children was assessed for the following elements when grading the strength of evidence.

**Consistency:** The majority of studies found no significant association between milk intake and adiposity measures in children. Of those studies that did find at least 1 significant association, the direction of effect was not consistent which supports “no association”. While only 4 studies examined the association between milk intake and height, 3 reported an association between milk intake and increased height. The one study that did not find a significant association had a duration of 12-weeks, and this may have been insufficient time to see an effect.

**Directness:** The population, intervention/exposure, comparators, and outcomes (PICO) of the body of evidence align with the elements outlined *a priori* in the Analytic Framework relatively well. However, the exposure of several cohort studies did not differentiate between levels of milk fat, which limits interpretation.

**Precision:** There were several large cohorts reporting consistency in associations; meanwhile, there were only 2 RCTs and although these were sufficiently powered, the sample sizes were small.

**Generalizability:** For the RCTs, given the design and sample size limitations, generalizability is low. Generalizability was stronger for the cohort studies, as there were several with large sample sizes, from different countries, and varying in age and duration.

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<sup>iii</sup> A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

**Risk of bias:** For the RCTs, the studies were considered low or moderate for risk of bias domains (see **Table 2** and **Table 3**). While one RCT found a difference between drinking milk and drinking water on adiposity outcomes, this effect was likely a result of drinking water not milk. For the prospective cohort studies, risk of bias was a concern. None of the studies accounted for all key confounders listed *a priori* in the Analytic Framework. Classification of exposures, missing data, and selection of reported results were also domains of concern.

## **Milk: Adults**

### ***Population***

The body of evidence in adults included 32 articles, with the mean baseline age ranging from approximately 26 years to 67 years old. Of the 7 RCTs, 4 studies were only in women, 1 study was only in men, and 2 studies included women and men. Across all studies, the majority were from the United States; however, several other high or very high HDI countries were represented, including: Australia, Canada, Denmark, Ecuador, Finland, France, Germany, Iran, Italy, Korea, Malaysia, the Netherlands, Spain, Sweden, and the UK. There were several large cohorts, and the overall analytic sample sizes ranged from 31 to 52,987. The predominant race/ethnic group represented in this evidence was non-Hispanic white; yet, there were 2 studies where more than half of participants at baseline were not non-Hispanic white.<sup>10,12</sup>

### ***Intervention/exposure and comparator***

The 7 RCTs used skim, 1%-fat, or low-fat milk as the intervention compared to either no milk or usual (low level) intake. The study durations ranged from 6 weeks to 2 years. Among the prospective cohort studies, approximately half defined the exposure generally as 'milk intake', whereas the other studies reported results based on at least one specific milk type (e.g., skim, whole, low-fat). The length of follow-up for the prospective cohort studies ranged from 16 weeks to 20 years.

### ***Outcomes***

In adults, weight status (prevalence or incidence of overweight or obesity), BMI, and body composition measures such as waist circumference, body fat, and abdominal adiposity were considered to reflect "adiposity". In adults, outcomes included weight, weight status, BMI, body fat, waist circumference, and waist-to-hip ratio.

### ***Evidence synthesis***

While about half of the studies indicated at least 1 significant effect or association, the vast majority of findings did not show significant associations between milk consumption in adults and weight-related outcomes. The significant associations that were reported were not consistent in direction of effect. Of the 7 RCTs, 2 reported at least 1 effect of milk intake leading to greater adiposity,<sup>5,57</sup> 2 reported an effect of milk intake and reduced adiposity,<sup>19,20</sup> and 3 reported no significant effects.<sup>12,13,38</sup> Results from the cohort studies were similar such that, approximately half did not report any significant findings; while the other studies found at least one significant association, the direction of effect was split. This inconsistency could not be explained after

consideration of a number of factors, including study design, exposure assessment and definition, outcome, or participant characteristics. The body of evidence had several strengths, including that the dose of milk consumed and length of follow-up were reasonable for testing this association. Further, several cohorts had very large sample sizes. Taken together, this body of evidence suggests there that is not an association between milk intake and adiposity in adults.

Of the 32 articles, only 2 reported height; both RCTs found no effect of milk intake on height in older adults over a 2-year intervention. The study by Chee et al<sup>12</sup> studied postmenopausal women in Malaysia. Daly et al<sup>13</sup> studied older white men in Australia.

Energy intake is an important covariate when interpreting studies on the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity because beverages might displace nutrient-dense foods or add additional energy to the diet. Therefore, findings with and without adjustments for energy intake were extracted and reviewed. Conclusion statements reflect the totality and strength of the evidence considering both approaches. Also, funding sources were documented during data extraction for consideration when reviewing this evidence. Further, publication bias is always a consideration in systematic reviews. This body of evidence includes both large and small studies and includes several studies that only report non-significant findings, therefore publication bias is not a serious concern.

### **Assessment of the evidence<sup>iv</sup>**

The conclusion statement “evidence suggests that milk intake is not associated with adiposity in *adults*” was assigned a grade of **limited**. As outlined and described below, the body of evidence examining milk consumption and growth, size, body composition, and risk of overweight and obesity in adults was assessed for the following elements when grading the strength of evidence.

**Consistency:** The majority of reported associations were not significant, and of the significant findings, the direction of effect was inconsistent.

**Directness:** The population, intervention/exposure, comparators, and outcomes of the body of evidence align with the elements outlined *a priori* in the Analytic Framework relatively well. However, the exposure of several cohort studies did not differentiate between levels of milk fat, which limits interpretation.

**Precision:** Precision was not a concern given that several studies had large sample sizes.

**Generalizability:** The population tested was large with some diversity, relatively generalizable to the US population.

**Risk of bias:** Risk of bias was a concern (see **Table 5** and **Table 6**). Few studies accounted for all key confounders listed *a priori* in the Analytic Framework. Other

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<sup>iv</sup> A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.



concerns were related to selection of participants, classification of exposures, missing data, self-reported outcome data, and no preregistered data analysis plan.

## **Research recommendations**

To address the limitations of this body of evidence, several research recommendations have been identified:

- Research on milk according to type of fat, showing results with and without adjustment for energy to see if there is an independent effect on adiposity
- Differentiate between different types of milk (fat & sweetener content)
- Trials that give participants a particular beverage as the intervention should give the control group a different beverage to test the effect of substituting one beverage for another.
- Assess the effects of lactose intolerance for certain racial/ethnic groups, such as African-, Asian- and Mexican-Americans, and/or to consider including lactose-free milk in research studies.

**Table 1: Summary of articles examining the relationship between milk consumption and growth, size, body composition and risk of overweight and obesity in children<sup>∨</sup>**

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
RANDOMIZED CONTROLLED TRIALS			

<sup>∨</sup> Abbreviations: adj: adjusted; AF: android fat; ANOVA: analysis of variance; BAZ: BMI-for-age; BF: body fat; BMI: body mass index; BMIZ: BMI z-score; Btwn: between; CDC: Center for Disease Control and Promotion; CI: confidence interval; d: day(s); DXA or DEXA: dual-energy X-ray absorptiometry; FFQ: food frequency questionnaire; FMI: fat mass index; GF: gynoid fat; HAZ: height-for-age z-score; LMI: lean mass index; MZ: monozygotic; N/A: not applicable; NHLBI: National Heart, Lung, and Blood Institute; NIH: National Institutes of Health; NR: not reported; NS: not significant; OR: odds ratio; Ovwt: overweight; RCT: randomized controlled trial; SD: standard deviation; SE: standard error; SES: socioeconomic status; TEI: total energy intake; unadj: unadjusted; USDA: U.S. Department of Agriculture; WC: waist circumference; WHO: World Health Organization; WHZ: weight-for-height z-score; wk: week(s); y: year(s)  
 Red font indicates a statistically significant detrimental relationship, and green font indicates a statistically significant beneficial relationship.

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Arnberg, 2012<sup>3</sup></b>  <b>RCT, Demark</b>            Baseline N=203, Analytic N=173            (Attrition: 15%); Power: recruit 200, 10% dropout expected, for diff of 0.4 SD or 1kg, <math>\alpha=0.05</math>, <math>\beta=80\%</math></p> <p><b>Recruitment:</b> all adolescents born 1995-1998 and living in the Copenhagen area invited to participate via post</p> <p><b>Participant characteristics: overweight adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~7525 kJ/d</li> <li>Sex (female): 62%</li> <li>Age, Mean (SD): 13.2 (0.7)y</li> <li>Race/ethnicity: Caucasian, 95%</li> <li>SES: NR</li> <li>Anthropometrics: BMI, <math>\leq 25</math>: 9.8%, 25.1-29.9: 78.8%, <math>\geq 30</math>: 11.4%</li> <li>Physical activity: NR (maintain usual level)</li> <li>Smoking: 100% non-smokers</li> </ul> <p><b>Summary of findings:</b>            In overweight adolescents, drinking skim milk (1 L/d) compared to water (1 L/d) for 12wk resulted in greater increases in BMI, BAZ, and weight but did not change waist circumference or waist to height ratio. Energy intake was greater during the intervention in the group that drank skim milk daily compared to water.</p>	<p><b>Intervention:</b> Skim milk (1 L/d), n=44</p> <p><b>Comparator:</b> Water (1 L/d), n=50</p> <p>Other interventions: whey drink, casein drink</p> <p><u>Intervention duration:</u> 12wk</p> <p><u>Intervention compliance:</u> percentage of planned intake actually consumed, skim milk 92%, water 95%</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Habitual milk/yogurt intake <math>\leq 250</math> mL/d (inclusion criteria)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 12wk follow-up</li> <li>Weight recorded in morning, after overnight fast on digital scale</li> <li>Height measured in triplicate</li> <li>Waist circumference at umbilicus level measured in triplicate</li> <li>BMI-for-age (BAZ), gender and age-specific Z-scores, calculated using WHO software</li> </ul> <p>Note: other outcomes reported in:</p> <ul style="list-style-type: none"> <li>Larnkjaer, 2015</li> <li>Larnkjaer, 2014</li> </ul>	<p><b>BMI</b>, kg/m<sup>2</sup>, Mean (SD), Linear regression  <b>Over time, within group:</b> 0wk, 12wk  <b>Water:</b> 25.2 (2.3), 25.5 (2.4); <math>P&lt;0.010</math>  <b>Skim milk:</b> 24.9 (2.5), 25.8 (2.8); <math>P&lt;0.001</math>  <b>Change over time, between groups:</b>  <b>Water:</b> 0.3 (0.8)  <b>Skim milk:</b> 0.6 (0.9), <math>P&lt;0.022</math></p> <p><b>BAZ</b>, Linear regression  <b>Change over time, within group:</b>            Water: <math>P=NS</math>, Data NR  <b>Skim milk:</b> <math>P=0.008</math>, Data NR  <b>Change over time, between groups:</b>  <b>Skim milk &gt; Water</b>, <math>P&lt;0.05</math>, Data NR</p> <p><b>Weight</b>, Linear regression  <b>Change over time, within group:</b>  <b>Water:</b> <math>P&lt;0.001</math>, Data NR  <b>Skim milk:</b> <math>P&lt;0.001</math>, Data NR  <b>Change over time, between groups:</b>  <b>Skim milk &gt; Water</b>, <math>P=0.032</math>, Data NR</p> <p><b>Waist circumference</b>, cm, Mean (SD), Linear regression  <b>Over time, within group:</b> 0wk, 12wk            Water: 85.3 (6.2), 86.0 (6.7); <math>P=NS</math>  <b>Skim milk:</b> 84.7 (7.7), 87.6 (8.6), <math>P=0.001</math>  <b>Change over time, between groups:</b>            Water: 0.7 (3.7)            Skim milk: 2.2 (4.2), <math>P=NS</math></p> <p><b>Waist to height ratio</b>, Mean (SD), Linear regression  <b>Over time, within group:</b> 0wk, 12wk            Water: 0.52 (0.04), 0.53 (0.04), <math>P=NS</math>  <b>Skim milk:</b> 0.52 (0.04), 0.54 (0.05), <math>P&lt;0.05</math>  <b>Change over time, between groups:</b>            Water: 0.00 (0.02)            Skim milk: 0.01 (0.03), <math>P=NS</math></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Energy Intake</b>, kJ/d, Mean (SD)  <b>EI, over time within group:</b> 0wk, 12wk  <b>Water:</b> 7620 (2100), 6700 (2450), <math>P=0.008</math>            Skim milk: 6980 (2390), 7360 (2130), <math>P=0.56</math>  <b>Change over time, between groups:</b>  <b>P=0.023</b>  <b>Water:</b> -920 (2330)  <b>Skim milk:</b> 100 (1980)</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, smoking, physical activity</li> <li>Other factors considered: total energy intake (no diff between groups at baseline), medications</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, supplements</li> </ul> <p><b>Additional model adjustments:</b>            Tanner stage</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Trial registry does not include data analysis plan</li> </ul> <p><b>Funding sources:</b>            Danish Agency for Science, Technology and Innovation; Danish Dairy Board</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Larnkjaer, 2014<sup>35</sup></b>  <b>RCT, Denmark</b>  Baseline N=203, Analytic N=193 (Attrition: 5%); Power: recruit 200, 10% dropout expected, for diff of 0.4 SD or 1kg, <math>\alpha=0.05</math>, <math>\beta=80\%</math></p> <p><b>Recruitment:</b> all adolescents born 1995-1998 and living in the Copenhagen area invited to participate via post</p> <p><b>Participant characteristics: overweight adolescents</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~7525 kJ/d</li> <li>• Sex (female): 62%</li> <li>• Age, y, mean (SD): 13.2 (0.7)</li> <li>• Race/ethnicity: 95% Caucasian</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI, <math>\leq 25</math>: 9.8%, 25.1-29.9: 78.8%, <math>\geq 30</math>: 11.4%</li> <li>• Physical activity: NR (maintain usual level)</li> <li>• Smoking: 100% non-smokers</li> </ul> <p><b>Summary of findings:</b>  In overweight adolescents, drinking skim milk (1 L/d) compared to water (1 L/d) for 12wk did not result in differences in changes of height or height z-score.</p>	<p><b>Intervention:</b> Skim milk (1 L/d), n=48</p> <p><b>Comparator:</b> Water (1 L/d), n=50</p> <p>Other interventions: whey drink, casein drink</p> <p><b>Intervention duration:</b> 12wk</p> <p><b>Intervention compliance:</b> percentage of planned intake actually consumed, skim milk 92<math>\pm</math>11%, water 95<math>\pm</math>7%</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Habitual milk/yogurt intake <math>\leq 250</math> mL/d (inclusion criteria)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 12wk follow-up</li> <li>• Height measured in triplicate and averaged to the nearest 0.01 cm.</li> <li>• Age- and sex-specific height z-score calculated using WHO Anthro 2007.</li> </ul> <p>Note: other outcomes reported in:</p> <ul style="list-style-type: none"> <li>• Larnkjaer, 2015</li> <li>• Arnberg, 2012</li> </ul>	<p><b>Height</b>, cm, Mean (SD), Linear regression  <b>Over time, within group:</b> 0wk, 12wk  Water: 162.93 (7.56), 163.89 (7.53), <math>P&lt;0.001</math>  Skim milk: 162.43 (7.52), 163.79 (7.19), <math>P&lt;0.001</math>  <b>Change over time, between groups:</b>  Water: 0.96 (0.80)  Skim milk: 0.92 (0.90)  <math>P=NS</math></p> <p><b>Height Z-score</b>, Mean (SD), Linear regression  <b>Over time, within group:</b> 0wk, 12wk  Water: 0.86 (0.95), 0.84 (0.94), <math>P=0.084</math>  Skim milk: 0.78 (0.87), 0.79 (0.85), <math>P=0.050</math>  <b>Change over time, between groups:</b>  Water: -0.02 (0.10)  Skim milk: -0.03 (0.10)  <math>P=NS</math></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, smoking, physical activity</li> <li>• Other factors considered: total energy intake (no diff between groups at baseline), medications</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Tanner stage, insulin like growth factor</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Trial registry does not include data analysis plan</li> </ul> <p><b>Funding sources:</b>  Danish Agency for Science, Technology and Innovation; Danish Dairy Board</p>

**Larnkjaer, 2015<sup>36</sup>****RCT, Denmark**

Baseline N=203, Analytic N=193  
(Attrition: 5%); Power: recruit 200, 10% dropout expected, for diff of 0.4 SD or 1kg,  $\alpha=0.05$ ,  $\beta=80\%$

**Recruitment:** all adolescents born 1995-1998 and living in the Copenhagen area invited to participate via post

**Participant characteristics: overweight adolescents**

- Total energy intake: Mean ~7525 kJ/d
- Sex (female): 62%
- Age, y, mean (SD): 13.2 (0.7)
- Race/ethnicity: Caucasian, 95%
- SES: NR
- Anthropometrics: BMI, Mean ~24.8 kg/m<sup>2</sup>:  $\leq 25$ : 9.8%; 25.1-29.9: 78.8%;  $\geq 30$ : 11.4%
- Physical activity: Pedometer counts ~9648; maintain usual activity
- Smoking: 100% non-smokers

**Summary of findings:**

In overweight adolescents, drinking skim milk (1 L/d) compared to water (1 L/d) for 12wk resulted in increased fat mass index. Both groups increased lean mass index over the 12 wk intervention, with no difference between groups. There were no differences between groups for android fat (%), gynoid fat (%), or android-gynoid fat ratio.

**Intervention:** Skim milk (1 L/d), n=48

**Comparator:** Water (1 L/d), n=50

Other interventions: whey drink, casein drink

Intervention duration: 12wk

Intervention compliance: percentage of planned intake actually consumed, skim milk 92%, water 95%

**Study beverage intake:**

- Habitual milk/yogurt intake  $\leq 250$  mL/d (inclusion criteria)

**Outcome assessment methods/timing:**

- At baseline, 12wk follow-up
- Total body fat (BF), lean mass, android fat (AF), and gynoid fat (GF) assessed using DEXA
- Fat mass index (FMI, fat mass/height<sup>2</sup>), lean mass index (LMI, lean mass/height<sup>2</sup>), and percentages of BF, AF, and GF were calculated from DEXA data
- Android fat:gynoid fat (AF/GF) ratio was calculated as android fat mass (g)/gynoid fat mass (g)

Note: other outcomes reported in:

- Larnkjaer, 2014
- Arnberg, 2012

**FMI**, kg/m<sup>2</sup>, Mean (SD), Linear regression  
**Over time, within group:** 0wk, 12wk  
Water: P=NS, Data NR

**Skim milk: P<0.05, Data NR**

**Change over time, between groups:**  
**Skim milk > Water, P<0.05, Data NR**

**LMI**, Mean (SD), Linear regression  
**Over time, within group:** 0wk, 12wk  
**Water: P<0.05, Data NR**  
**Skim milk: P<0.05, Data NR**  
**Change over time, between groups:**  
P=NS

**AF%**, Mean (SD), Linear regression  
**Change over time, within group:** 0wk, 12wk  
Water: 8.19 (0.73), 8.14 (0.81), P=0.346  
Skim milk: 8.23 (0.96), 8.23 (0.90), P=0.646  
**Change over time, between groups:**  
Water: -0.05 (0.39)  
Skim milk: 0.03 (0.43)  
P=0.265

**GF%**, Mean (SD), Linear regression  
**Change over time, within group:** 0wk, 12wk  
Water: 19.2 (1.7), 19.4 (1.8), P=0.112  
Skim milk: 19.0 (1.8), 19.0 (1.8), P=0.918  
**Change over time, between groups:**  
Water: 0.18 (0.77)  
Skim milk: -0.07 (0.80)  
P=0.211

**AF/GF ratio**, Mean (SD), Linear regression  
**Change over time, within group:** 0wk, 12wk  
Water: 0.43 (0.06), 0.43 (0.07), P=0.057  
Skim milk: 0.44 (0.08), 0.44 (0.08), P=0.656  
**Change over time, between groups:**  
Water: -0.01 (0.02)  
Skim milk: 0.00 (0.02)  
P=0.095

**TEI adjusted:** No

**Confounders accounted for:**

- Key confounders: sex, age, anthropometry at baseline, smoking, physical activity
- Other factors considered: total energy intake (no diff between groups at baseline), medications

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity, SES
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, supplements

**Additional model adjustments:**

Tanner stage, leptin

**Limitations:**

- Trial registry does not include data analysis plan

**Funding sources:**

Danish Agency for Science, Technology and Innovation; Danish Dairy Board

## **Lambourne, 2013**<sup>34</sup>

### **RCT, United States**

Baseline N=136, Analytic N=108  
(Attrition: 21%); Power: Achieved sample size gives 80% power to detect medium difference (Glass's delta = 0.75) in FFM among groups with alpha = 0.05, assuming correlation between repeated measures up to 0.60

**Recruitment:** convenience sample from middle school physical education programs

### **Participant characteristics: adolescents participating in resistance training intervention**

- Total energy intake: Mean ~1564 kcal/d
- Sex (female): 64%
- Age: Mean ~13.6y
- Race/ethnicity: 86% minorities
- SES: NR
- Anthropometrics: BMI percentile, mean, ~85
- Physical activity: Moderate to vigorous physical activity, Mean ~25 min/d; All participating in resistance training for RCT
- Smoking: NR

### **Summary of findings:**

In adolescents participating in a resistance training intervention, consumption of 24 fl oz of milk/d for 6mo compared to 24 fl oz of water/d did not result in differences in body mass, fat mass, fat free mass, percent body fat, BMI percentile, or waist circumference.

**Exposure of interest:** Milk (24 fl oz/d of fat-free chocolate milk and 1% fat white milk; resistance training 3d/wk), n=36 (Boys, n=13; Girls, n=23)

**Comparator:** Water (24 fl oz/d bottled water; resistance training 3d/wk), n=38 (Boys, n=12; Girls, n=26)

Other interventions: juice

Intervention duration: 6mo

Intervention compliance: Directly observed by study staff on weekdays and obtained by self-report on weekends; Mean (SD) supplements consumed: Milk 83.9% (9.2), Water 89.8% (5.8)

### **Study beverage intake:**

- Milk: Mean ~0.7 svg/d

### **Outcome assessment methods/timing:**

- At baseline, 6mo
- Height and weight measured by trained research staff
- BMI percentile calculated using CDC software
- Waist circumference measured by trained research staff using procedures of Lohman, Roche, and Martorell (1988)
- Fat Mass (FM), Fat-free mass (FFM), and % body fat: assessed via DXA

**Body mass**, kg, Mean (SD), Linear mixed model

By study group: baseline, 6mo change

Water: 62.8 (13.8), 2.3 (2.9)

Milk: 63.7 (11.2), 3.4 (3.7)

Group, P=0.12; **Time, P<0.0001**

### **Boys**

Water: 65.1 (13.8), 2.8 (3.3)

Milk: 65.7 (9.8), 5.2 (3.9)

Group, P=0.14; **Time, P<0.0001**

### **Girls**

Water: 61.8 (14.0), 2.0 (2.8)

Milk: 62.7 (12.0), 2.3 (3.2)

Group, P=0.60; **Time, P<0.0001**

**Fat mass**, kg, Mean (SD), Linear mixed model

By study group: baseline, 6mo change

Water: 20.9 (10.2), 0.4 (3.6)

Milk: 20.8 (8.1), 1.1 (2.8)

Group, P=0.33; **Time, P<0.0001**

### **Boys**

Water: 17.4 (10.6), -1.9 (4.7)

Milk: 17.5 (7.2), 1.3 (2.9)

Group, P=0.04; Time, P=0.06

Pairwise comparison, P=0.054

Per protocol analysis, P=NS

### **Girls**

Water: 22.5 (9.8), 1.5 (2.5)

Milk: 22.6 (8.2), 1.0 (2.8)

Group, P=0.85; **Time, P<0.0001**

**Fat free mass**, kg, Mean (SD), Linear mixed model

By study group: baseline, 6mo change

Water: 41.4 (8.6), 1.7 (2.9)

Milk: 42.3 (7.3), 2.2 (1.9)

Group, P=0.06; **Time, P<0.0001**

### **Boys**

Water: 47.9 (9.7), 4.3 (1.4)

Milk: 47.7 (7.4), 3.9 (1.6)

Group, P=0.99; **Time, P<0.0001**

### **Girls**

Water: 38.4 (9.7), 0.5 (1.3)

Milk: 39.3 (5.3), 1.2 (1.5)

Group, P=0.25; Time, P=0.49

**TEI adjusted:** No

**Energy intake**, kcal/d, Mean

Change by study group:

Control: -16

Milk: 337

**Between groups, P=0.01**

### **Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity
- Other factors considered: none

### **Confounders NOT accounted for:**

- Key confounders: SES, smoking
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

### **Additional model adjustments:**

Study site

### **Limitations:**

- No information on randomization and concealment of allocation sequence
- No preregistered data analysis plan

### **Funding source:**

Dairy Research Institute

**Percent fat**, %, Mean (SD), Linear mixed model

By study group: baseline, 6mo change

Water: 33.5 (11.0), 0 (3.5)

Milk: 33.9 (9.6), -0.2 (3.3)

Group, P=0.99; Time, P=0.05

***Boys***

Water: 25.6 (11.0), -2.8 (3.2)

Milk: 27.4 (9.6), -0.2 (3.3)

Group, P=0.05; Time, P=0.87

Pairwise comparison, P=0.059

***Girls***

Water: 37.2 (11.0), 1.3 (2.9)

Milk: 37.5 (7.7), -0.1 (3.3)

Group, P=0.22; **Time, P=0.01**

**BMI percentile**, Mean (SD), Linear mixed model

By study group: baseline, 6mo change

Water: 84.7 (12.7), 0.3 (7.1)

Milk: 83.9 (14.7), 0.9 (7.3)

Group, P=0.56; **Time, P<0.0001**

***Boys***

Water: 85.6 (12.7), -2.0 (4.5)

Milk: 85.4 (14.7), 1.9 (8.9)

Group, P=0.07; **Time, P=0.04**

***Girls***

Water: 84.3 (12.7), 1.4 (7.9)

Milk: 83.0 (15.1), 0.3 (6.3)

Group, P=0.94; **Time, P<0.0001**

**WC**, cm, Mean (SD), Linear mixed model

By study group: baseline, 6mo change

Water: 77.3 (9.3), 0.6 (4.2)

Milk: 76.9 (8.9), 1.2 (3.1)

Group, P=0.20; Time, P=0.67

***Boys***

Water: 79.0 (10.3), 0.9 (5.2)

Milk: 79.2 (8.1), 2.1 (3.6)

Group, P=0.21; Time, P=0.85

***Girls***

Water: 76.6 (8.9), 0.4 (3.8)

Milk: 75.6 (9.2), 0.7 (2.8)

Group, P=0.25; Time, P=0.49

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<b>PROSPECTIVE COHORT STUDIES</b>			
<p><b>Berkey, 2004<sup>7</sup></b>  <b>Prospective Cohort Study, Growing Up Today Study, United States</b>            Baseline N=16,771, Analytic N=11,654 (Attrition: 31%); Power: NR</p> <p><b>Recruitment:</b> convenience sample (children of NHSII participants)</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Boys, Mean~2290 kcal/d; Girls, Mean~2050 kcal/d</li> <li>Sex (female): ~57%</li> <li>Age: Range: 9-14 y</li> <li>Race/ethnicity: White, 94.7%</li> <li>SES: NR</li> <li>Anthropometrics: Overweight (&gt;85<sup>th</sup> percentile CDC BMI charts): boys: 23.2%; girls: 17.5%; Very lean (&lt;10<sup>th</sup> percentile): boys: 7.2%; girls: 8.6%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            There was not a significant association between a change in the number of daily milk servings and change in BMI over 1y in children 9-14 y of age.</p>	<p><b>Exposure of interest:</b> Milk (white, in a glass or on cereal, and chocolate)</p> <p><b>Comparator:</b> Milk intake (change in milk intake over 1 y period; continuous; svg/d)</p> <p>Other exposures: sugar-added beverages, diet soda, fruit juices</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Self-administered semi-quantitative, validated FFQ for older children and adolescents; Represents intake during previous year</li> <li>At baseline, 1y follow-up, 2y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk intake (boys): Mean ~2.21 svg/d</li> <li>Milk intake (girls): Mean ~1.88 svg/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 1y follow-up, 2y follow-up</li> <li>BMI from height and weight self-reported by children with measuring instructions and suggestion to ask someone for help provided (all have mothers who are nurses in NHSII)</li> </ul>	<p><b>Milk intake, continuous BMI change over 1y</b>, kg/m<sup>2</sup>, <math>\beta</math> (SE), Linear regression            Per 1y svg/d increase:  <b>Not adjusted for TEI</b>            Boys: 0.028 (0.015), P=0.054            Girls: 0.019 (0.013), P=0.153  <b>Adjusted for TEI</b>            Boys: 0.016 (0.016), P=0.323            Girls: 0.016 (0.014), P=0.250</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Tanner stage, menarche (girls), height growth, milk type, inactivity, other beverage intake (sugar added, diet soda, fruit juices)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Children lost to follow-up were older and had higher sugar added beverage intake and lower milk intake at baseline</li> <li>Self-reported height and weight</li> <li>Sugar-added beverage analyses differ from analyses for other beverage types</li> <li>No preregistered protocol</li> </ul> <p><b>Funding sources:</b>            NIH; Boston Obesity Nutrition Research Center Grant; CDC; Economic Research Service of the USDA; Kellogg's</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b><u>Berkey, 2005<sup>8</sup></u></b>  <b>Prospective Cohort Study, Growing Up Today Study, United States</b>  Baseline N=16,771, Analytic N=13,514 (Attrition: 19%); Power: NR</p> <p><b>Recruitment:</b> convenience sample (children of NHSII participants)</p> <p><b>Participant characteristics: children/adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Boys, Mean~2290 kcal/d; Girls, Mean~2050 kcal/d</li> <li>Sex (female): ~56%</li> <li>Age: Range: 9-14 y</li> <li>Race/ethnicity: White, 94.7%</li> <li>SES: NR</li> <li>Anthropometrics: Overweight (85<sup>th</sup> to 95<sup>th</sup> percentile CDC BMI charts): boys: 14.6%; girls: 12.7%; Obese (&gt;95<sup>th</sup> percentile): boys: 8.7%; girls: 4.8%; Very lean (&lt;5<sup>th</sup> percentile): boys: 4.2%; girls: 4.7%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, change in milk intake was not significantly associated with BMI change. Typical milk intake was not associated with incident overweight after 3y of follow-up.</p>	<p><b>Exposure of interest:</b> Milk (white, in a glass or on cereal, and chocolate)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Milk intake (change in milk intake over 1 y period; continuous; svg/d)</li> <li>Milk intake (typical consumption over whole study period; categorical; svg/d) <ul style="list-style-type: none"> <li>&gt;1 and ≤2</li> <li>&gt;2 and ≤3</li> <li>&gt;3</li> </ul> </li> </ul> <p>Other exposures: milk intake by fat amount (analyses do not meet study design I/E), calcium</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Self-administered semi-quantitative, validated FFQ for older children and adolescents and abbreviated FFQ at 3y follow-up; Represents intake during previous year</li> <li>At baseline, 1y follow-up, 2y follow-up, 3y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk intake (svg/d), boys: Mean=2.2</li> <li>Milk intake (svg/d), girls: Mean=1.9</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 1y follow-up, 2y follow-up, 3y follow-up</li> <li>BMI from height and weight self-reported by children with measuring instructions and suggestion to ask someone for help provided (all have mothers who are nurses in NHSII)</li> </ul>	<p><b>Milk intake, continuous BMI change over 1y</b> Per 1y svg/d increase, kg/m<sup>2</sup>, β (SE), Linear regression:  <b>Boys</b> (n=5961): 0.023, P=0.08  <b>Girls</b> (n=7553): 0.023, P=0.05</p> <p><b>Milk intake, categorical BMI change over 3y</b>, kg/m<sup>2</sup>, β (SE), Linear regression; N=9166 (children who returned survey all 4 yrs)  <b>Boys</b>  &gt;2 and ≤3 svg/d (ref; n=499) vs &gt;3 svg/d (n=129): 0.262, P=0.19  <b>Girls</b>  &gt;2 and ≤3 svg/d (ref; n=652) vs &gt;3 svg/d (n=129): 0.213, P=0.24</p> <p><b>Incident overweight</b>, RR (95% CI), Logistic regression; N=NR  Between group differences:  <b>Boys</b>  &gt;1 and ≤2 svg/d (ref) vs &gt;3 svg/d: 1.35 (0.96, 1.90)  &gt;2 and ≤3 svg/d (ref) vs &gt;3 svg/d: 1.26 (0.95, 1.66)  <b>Girls</b>  &gt;1 and ≤2 svg/d (ref) vs &gt;3 svg/d: 1.36 (0.92, 2.01)  &gt;2 and ≤3 svg/d (ref) vs &gt;3 svg/d: 1.25 (0.91, 1.72)</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Prior milk intake, same-year height growth, tanner stage, menstrual history (girls), same-year inactivity (TV/videos/computer games)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Self-reported height and weight</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH; Boston Obesity Nutrition Research Center Grant; CDC; Economic Research Service of the USDA; Kellogg's; Breast Cancer Research Foundation</p>

## **Berkey, 2009<sup>6</sup>**

### **Prospective Cohort Study, Growing Up Today Study, United States**

Baseline N=5556, Analytic N=5101  
(Attrition: 8%) Power: NR

**Recruitment:** convenience sample  
(daughters of NHSII participants)

#### **Participant characteristics: girls**

- Total energy intake: NR
- Sex (female): 100%
- Age: Mean ~11.2 y
- Race/ethnicity: Non-Hispanic White, ~95%
- SES: NR
- Anthropometrics: BMI, ~18.2; Height, ~57.8 in
- Physical activity: NR
- Smoking: NR

#### **Summary of findings:**

Greater milk intake was associated with greater height growth, PHV, and adult height in girls.

**Exposure of interest:** Milk (white, in a glass or on cereal, and chocolate)

#### **Comparators:**

- White milk intake (categorical; svg/d)
  - <1 (ref)
  - >3
- Milk intake (white + chocolate; continuous; svg/d)

Other exposures: cheese, yogurt

#### **Exposure assessment method and timing:**

- Self-administered, semi-quantitative, validated FFQ for older children and adolescents; Represents intake during previous year
- At baseline, annually for 5y

#### **Study beverage intake:**

- Milk intake (glasses/d): 0-<1: 32.1%; 1: 20.4%; 2-3: 36.6%; >3: 10.9%
- Milk intake (glasses/d): Mean ~1.9
- Chocolate milk intake (glasses/wk): >1: 20%

#### **Outcome assessment methods/timing:**

- At baseline, annually for 5y
- Annualized height growth from self-reported heights by children with measuring instructions and suggestion to ask someone for help (all have mothers who are nurses in NHSII)
- Peak height velocity (PHV) defined as largest annualized height growth
- Adult height defined as greatest height attained after onset of menses

*White milk intake, categorical*  
**Height growth**, in, Beta, Linear regression

1y change in height by preceding white milk intake, between group difference (N=5070):

**Not adjusted for TEI**

<1 svg/d (ref) vs >3 svg/d: **0.112, P=0.007**

**Adjusted for TEI**

<1 svg/d (ref) vs >3 svg/d: **0.108, P=0.017**

**PHV**, in, Beta, Linear regression

By baseline white milk intake, between group difference (N=5022):

**Not adjusted for TEI**

<1 svg/d (ref) vs >3 svg/d: **0.159, P=0.004**

**Adjusted for TEI**

<1 svg/d (ref) vs >3 svg/d: **0.140, P=0.014**

**Adult height**, in, Beta, Linear regression

By baseline white milk intake, between group difference (N=4870):

**Not adjusted for TEI**

<1 svg/d (ref) vs >3 svg/d: **0.317, P=0.001**

**Adjusted for TEI**

<1 svg/d (ref) vs >3 svg/d: **0.297, P=0.003**

*Milk intake (white + chocolate), continuous*

**All adjusted for TEI**

**Height growth**, in, Beta, Linear regression

1y change in height per svg/d increase in preceding milk intake (N=5024):

**0.024, P=0.019**

**PHV**, in, Beta, Linear regression

Per svg/d increase in baseline milk intake (N=4975):

**0.039, P=0.003**

**Adult height**, in, Beta, Linear regression

Per svg/d increase in baseline milk intake (N=4829):

**0.076, P=0.001**

**TEI adjusted:** Yes and No

#### **Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, anthropometry at baseline
- Other factors considered: total energy intake

#### **Confounders NOT accounted for:**

- Key confounders: SES, physical activity, smoking
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:** Tanner stage (adult height analyses only), cheese intake, yogurt intake

#### **Limitations:**

- Not all key confounders accounted for
- Self-reported height
- No preregistered data analysis plan

#### **Funding sources:**

NIH; The Breast Cancer Research Foundation

**Blum, 2005<sup>11</sup>**

**Prospective Cohort Study, United States**

Baseline N=830, Analytic N=166  
(Attrition: 80%) Power: NR

**Recruitment:** convenience sample of elementary school children in grades 3 through 6 who had participated in a previous study

**Participant characteristics: children**

- Total energy intake: Mean=1957.7 kcal/d, SD=575.3
- Sex (female): 55.4%
- Age: Mean=9.3 y, SD=1.0
- Race/ethnicity: Caucasian, ~94%
- SES: NR
- Anthropometrics: BMI z-score, Mean=0.47, SD=1.0; Height, Mean=139.4 cm, SD=7.9; Weight, Mean=35.7 kg, SD=8.1
- Physical activity: NR
- Smoking: NR

**Summary of findings:**

Children who remained "normal weight" after 2 years, consumed less milk at the 2 year follow-up compared to baseline. However, there was no difference in milk intake change over 2 years among children who remained overweight or children who changed from normal to overweight or overweight to normal weight. Change in milk intake did not vary by BMIZ group. Overall, child milk intake at baseline was not significantly associated with BMI z-score two years later.

**Exposure of interest:** Milk (skim, 1%, 2%, whole, chocolate, milkshakes)

**Comparator:** Milk intake (continuous; oz/d)

Other exposures: 100% juice, diet soda, sugar sweetened drinks

Exposure assessment method and timing:

- 24-hr recall with two interviews per 24-hr period; parents of random sub-sample called to verify consumption at home; Represents intake during past 24-hr on school days
- At baseline and 2y follow-up

**Study beverage intake:**

- Milk (oz/d): Mean=19.5, SD=12.0

**Outcome assessment methods/timing:**

- At baseline and 2y follow-up
- Weight and height measured
- BMI z-score calculated (CDC age and gender specific) from height and weight; Overweight: BMIZ  $\geq 1.0$ ; Normal weight: BMIZ  $< 1.0$

**Milk intake, continuous**

Change in Milk intake for Change-in-BMIZ subgroups, oz/d; Mean (SD):

**Unadjusted analysis**

Within group differences (t-tests):

Normal wt at baseline & 2y, n=99: -3.3 (14.4), P<0.05

Overweight at baseline & 2y, n=48: -3.5 (15.0), P=NS

Gained wt (Normal wt at baseline; Ovwt at 2y), n= 11: -2.8 (10.1), P=NS

Lost wt (Ovwt at baseline; Normal wt at 2y), n= 6: -4.3 (10.4), P=NS

Between group differences (ANOVA): All NS

BMI z-score, Increase per oz/d increase in baseline intake, linear regression: P=NS, Data: NR

**TEI adjusted:** Yes

**Change in TEI for Change-in-BMIZ subgroups, kcal/d; ANOVA, Mean (SD):**

Within group differences:

Normal wt at baseline & 2y, n=99: -118.4 (724.9), P<0.05

Overweight at baseline & 2y, n=48: -165.1 (693.1), P=NS

Gained wt (Normal wt at baseline; Ovwt at 2y), n=11: -173.6 (592.0), P=NS

Lost wt (Ovwt at baseline; Normal wt at 2y), n= 6: 140.3 (920), P=NS

Between group differences: All NS

**Confounders accounted for:**

- Key confounders: sex, age, anthropometry at baseline,
- Other factors considered: total energy intake

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity, SES, physical activity, smoking
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:** Baseline beverage intakes, 2y follow-up beverage intakes

**Limitations:**

- Not all key confounders accounted for
- Single 24-hr recall used to assess intake
- Impact of high level of missing data on analyses unclear
- No preregistered analysis plan

**Funding sources:**

NR

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>DeBoer, 2015<sup>14</sup></b>  <b>Prospective Cohort Study, Early Childhood Longitudinal Survey-Birth Cohort, United States</b>            Baseline N=10,700, Analytic N=7,000 (Attrition: 35%) Power: NR</p> <p><b>Recruitment:</b> nationally-representative random sample of birth certificates</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49.2%</li> <li>Age: ~4 y</li> <li>Race/ethnicity: White 43.7%, Black 15.4%, Hispanic 19.7%, Asian 10.1%, Other 11.1%</li> <li>SES: High 23.2%, Medium High 19.8%, Medium 19.9%, Medium Low 19.0%, Low 18.1%</li> <li>Anthropometrics: Normal weight (&lt;85<sup>th</sup> %) 67.7%, Overweight (&gt;85<sup>th</sup>-95<sup>th</sup> %) 16.3%, Obese (&gt;95<sup>th</sup> %) 16.0%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            Higher milk intake at 4 y was associated with higher HAZ at 5y, but was not associated with BMI z-score or WHZ. Increasing fat content of milk typically consumed at 4 y was associated with lower BMI z-score, HAZ, and WHZ.</p>	<p><b>Exposure of interest:</b> Milk (all types of milk from a glass, cup or carton, or with cereal)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Milk intake (continuous; svg/d)               <ul style="list-style-type: none"> <li>Excluding non-milk drinkers</li> </ul> </li> <li>Milk intake (categorical; svg/d)               <ul style="list-style-type: none"> <li>Excluding non-milk drinkers</li> <li>Svg/d: &lt;1, 1, 2, 3, &gt;4</li> </ul> </li> <li>Milk type (continuous; svg/d)               <ul style="list-style-type: none"> <li>Increasing fat content</li> </ul> </li> </ul> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Two questions (amount and type) asked via computer-assisted interview overseen by trained assessor; Represents past 7d</li> <li>At baseline (4y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk intake (svg/d):               <ul style="list-style-type: none"> <li>None: boys: 2.6%; girls: 2.1%</li> <li>2-3: 53%</li> </ul> </li> <li>Milk type normally consumed: whole milk 43.2%, 2% milk 40.1%, 1% milk 8.1%, skim milk 6.6%, soy milk 2.0%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>1y follow-up (at 5yo)</li> <li>Weight and height measured by trained researchers</li> <li>BMI z-score, HAZ, and WHZ generated via computer program using CDC age and gender specific growth measures</li> <li>Overweight defined as &gt;85<sup>th</sup>-95<sup>th</sup> % BMI z-score</li> <li>Obesity defined as &gt;95<sup>th</sup> % BMIZ</li> </ul>	<p><b>Milk intake, continuous:</b> Per svg/d increase in baseline intake; <math>\beta</math> (SE) linear regression  <b>BMI z-score:</b> 0.006 (0.023), P=0.789  <b>HAZ:</b> 0.075 (0.0166), P&lt;0.001  <b>WHZ:</b> 0.0224 (0.0189), P=0.240</p> <p><b>Milk intake, categorical:</b> <math>\leq 2</math> svg/d (ref) vs <math>\geq 3</math> svg/d: OR (95% CI), logistic regression  <b>Overweight:</b> 1.094 (0.917, 1.306), P=0.3187  <b>Obesity:</b> 1.047 (0.863, 1.269), P=0.6427</p> <p>Adjusted mean z-scores among milk drinkers based on 4y intake on 5y outcomes: linear regression  <b>BMI z-score:</b> Data NR, P=NS  <b>HAZ:</b> &lt;1 svg/d (ref) vs 2, 3, or &gt;4 svg/d, Data NR, P&lt;0.05  <b>1 svg/d (ref) vs 2 or &gt;4 svg/d, Data NR, P&lt;0.05;</b> vs 3 svg/d, Data NR, P=NS  <b>WHZ:</b> Data NR, P=NS</p> <p><b>Milk type, continuous:</b> Per increase in fat content of milk normally consumed at baseline; <math>\beta</math> (SE) linear regression  <b>BMI z-score:</b> -0.139 (0.034), P&lt;0.001  <b>HAZ:</b> -0.147 (0.030), P&lt;0.001  <b>WHZ:</b> -0.145 (0.027), P&lt;0.001</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Assessment of milk intake not validated</li> <li>Impact of missing data on analyses unclear</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>            NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Dong, 2015<sup>15</sup></b>  <b>Prospective Cohort Study, Avon Longitudinal Study of Parents and Children (ALSPAC), UK</b>  Baseline N=15,444 (recruited), Analytic N=4,646 (Attrition: 70%) Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49.2%</li> <li>Age: Mean=7.5y</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI, Mean=16.2; BMI z-score, Mean=0.1</li> <li>Physical activity: Mean=22.9 min/d, SD=15.4 (at 11y)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Among children, increases in full-fat and low-fat milk intake over a 3y period were associated with excessive weight gain (increase in BMI z-score). Average intake of full-fat and low-fat milk intake over 3y was not significantly associated with excessive weight gain (increase in BMI z-score).</p>	<p><b>Exposure of interest:</b> Full-fat milk (full-fat milk, other milk and cream), Low-fat milk (semi-skimmed milk, skimmed milk, soya milk)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Full-fat milk (continuous; g/d) <ul style="list-style-type: none"> <li>Per 100 g/d change over 3y</li> <li>Per 100 g/d average across 3y</li> </ul> </li> <li>Low-fat milk (continuous; g/d) <ul style="list-style-type: none"> <li>Per 100 g/d change over 3y</li> <li>Per 100 g/d average across 3y</li> </ul> </li> </ul> <p>Other exposures: sugar-sweetened beverages, juices, diet soda</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Three-day food diary, child report with help from parent; Represents current intake</li> <li>At 7y, 10y, and 13y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Full-fat milk (g/d), mean (SD): 7y: 133.3 (182.0); 10y: 74.0 (146.7); 13y: 48.3 (138.4)</li> <li>Low-fat milk (g/d), mean (SD): 7y: 125.4 (167.1); 10y: 144.6 (170.7); 13y: 168.5 (195.1)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At 7y, 10y, and 13y</li> <li>Height and weight measured by study personnel</li> <li>Calculated UK age and sex adjusted BMI z-score to represent adiposity</li> <li>Excessive weight gain: increase in adiposity over 3y compared to reference group</li> <li>BMI converted to g for interpretation (assumes 0.01 increase in BMI=50g)</li> </ul>	<p><b>Excess weight gain (g) over 3y</b>, per 100 g/d increase (change) or per 100 g/d intake (average), Mean, linear regression</p> <p><b>Full-fat milk intake, continuous</b>  <b>Change: 65, P&lt;0.01</b>  Average: -40, P&lt;0.10  <b>By sex:</b>  Boys (n=2155)  <b>Change: 55, P&lt;0.05</b>  Girls (n=2193)  <b>Change: 80, P&lt;0.05</b>  <b>Change from 7-10y: 79, P&lt;0.01</b>  <b>Change from 10-13y: 95, P&lt;0.01</b></p> <p><b>Low-fat milk intake, continuous</b>  <b>Change: 40, P&lt;0.05</b>  Average: -40, P&lt;0.10  Boys (n=2155)  Change: 19, P=NS  Girls (n=2193)  <b>Change: 76, P&lt;0.05</b>  <b>Change from 7-10y: 64, P&lt;0.05</b>  <b>Change from 10-13y: 39, P=NS</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, physical activity</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, anthropometry at baseline, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Puberty status (Tanner stage)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Impact of missing data on analyses unclear</li> <li>Results from subgroup analyses are only report for change data, not average intake data which may show fewer/no significant associations</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NR</p>

## **DuBois, 2016<sup>17</sup>**

### **Prospective Cohort Study, Quebec Newborn Twin Study, Canada**

Baseline N=1324, Analytic N=304  
(Attrition: 77%); Power NR

#### **Participant characteristics: monozygotic (MZ) twin children**

- Total energy intake, Mean (SD): 1814.37 kcal/d (393.20)
- Sex (female): 54.6%
- Age, Mean (SD): 8.96 y (0.56)
- Race/ethnicity: NR
- SES: NR
- Anthropometrics, Mean (SD): BMI, 16.51 (2.50)
- Physical activity: NR
- Smoking: NR

#### **Summary of findings:**

Differences between MZ twin pairs' milk intake at 9y, particularly low-fat milk, was associated with differences in BMI (greater milk intake, larger increase in BMI).

**Exposure of interest:** Milk, High-fat milk, Low-fat milk, Milk and alternatives, High-fat milk and alternatives, Low-fat milk and alternatives

#### **Comparators:**

- Milk intake (continuous; kcal and % of energy)
- High-fat milk intake (continuous; kcal and % of energy)
- Low-fat milk intake (continuous; kcal and % of energy)
- Milk and alternatives intake (continuous; kcal and % of energy)
- High-fat milk and alternatives intake (continuous; kcal and % of energy)
- Low-fat milk and alternatives intake (continuous; kcal and % of energy)

Other exposures: fruit juice, sugary drinks, fruit drinks, soft drinks

#### **Exposure assessment method and timing:**

- 24-hr recall performed by registered dietitians; Represents usual intake
- At baseline (9y)

#### **Study beverage intake, kcal, Mean (SD)**

- Milk: 167.04 (128.42)
- High-fat milk: 25.76 (83.02)
- Low-fat milk: 141.29 (118.45)
- Milk and alternatives: 318.72 (154.99)
- High-fat milk and alternatives: 147.25 (126.10)
- Low-fat milk and alternatives: 171.47 (125.81)

#### **Outcome assessment methods/timing:**

- At baseline (9y), 12y, 13y, 14y
- Height and weight self-reported except at baseline (measured)
- Intrapair difference (MZ twins) in BMI

#### **Milk intake, continuous**

**Correlation between intrapair differences in intake at 9y (kcal or % energy) and intrapair differences in BMI in subsequent yrs; Spearman correlation**

**All: kcal; % energy**

**12y** (n=238): 0.13; 0.10

**13y** (n=226): 0.10; 0.09

**14y** (n=212): 0.12; 0.14

**Change 9-14y** (n=210): 0.16, P<0.10;

**0.13, P<0.05**

**Boys: kcal; % energy**

**12y** (n=102): 0.02; -0.01

**13y** (n=96): 0.11; 0.09

**14y** (n=92): 0.05; 0.10

**Change 9-14y** (n=92): -0.06; 0.01

**Girls: kcal; % energy**

**12y** (n=136): 0.20, P<0.10; 0.19

**13y** (n=130): 0.12; 0.14

**14y** (n=120): 0.19; 0.24, P<0.10

**Change 9-14y** (n=108): **0.37, P<0.05; 0.45, P<0.05**

#### **High-fat milk intake, continuous**

**Correlation between intrapair differences in intake at 9y (kcal or % energy) and intrapair differences in BMI in subsequent yrs; Spearman correlation**

**All: kcal; % energy**

**12y** (n=238): 0.06; 0.05

**13y** (n=226): -0.08; -0.08

**14y** (n=212): 0.06; 0.06

**Change 9-14y** (n=210): -0.04; -0.03

**Boys: kcal; % energy**

**12y** (n=102): 0.21; 0.21

**13y** (n=96): 0.05; 0.05

**14y** (n=92): 0.09; 0.10

**Change 9-14y** (n=92): -0.13; -0.12

**Girls: kcal; % energy**

**12y** (n=136): -0.06; -0.07

**13y** (n=130): -0.17; -0.18

**14y** (n=120): 0.07; 0.06

**Change 9-14y** (n=108): 0.05; 0.06

**TEI adjusted:** Yes (% energy) and No

**Correlation between MZ twin pair differences in BMI and TEI (kcal), Spearman correlation**

**12y: 0.07; 13y: 0.10; 14y: 0.07**

**Change 9-14y: 0.00**

#### **Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, SES,
- Other factors considered: none

#### **Confounders NOT accounted for:**

- Key confounders: anthropometry at baseline, physical activity, smoking
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:** N/A

#### **Limitations:**

- Not all key confounders accounted for
- Start of follow-up and exposure do not coincide
- 77% attrition with no information on those lost to follow-up
- Weight and height self-reported
- No pre-registered data analysis plan

#### **Funding sources:**

Fonds Quebecois de la Recherche sur la Societe et la Culture; Fonds de la Recherche en Sante du Quebec; Social Science and Humanities Research Council of Canada; National Health Research Development Program; CIHR; Sainte-Justine Hospital Research Centre; Academy of Finland

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
	<ul style="list-style-type: none"> <li>Discordant twins defined as <math>\geq 2</math> BMI units between pairs at least once at 9, 12, 13, and/or 14y</li> <li>Concordant twins defined as <math>&lt; 2</math> BMI units between pairs at all ages</li> </ul>	<p><b><u>Low-fat milk intake</u>, continuous</b></p> <p><b>Correlation between inpair differences in intake at 9y (kcal or % energy) and inpair differences in BMI in subsequent yrs; Spearman correlation</b></p> <p><b>All: kcal; % energy</b></p> <p><b>12y</b> (n=238): 0.10; 0.10</p> <p><b>13y</b> (n=226): kcal: 0.12; 0.11</p> <p><b>14y</b> (n=212): kcal: 0.12; 0.14</p> <p><b>Change 9-14y</b> (n=210): 0.18, <math>P &lt; 0.10</math>; <b>0.24, <math>P &lt; 0.05</math></b></p> <p><b>Boys: kcal; % energy</b></p> <p><b>12y</b> (n=102): -0.05; -0.08</p> <p><b>13y</b> (n=96): 0.11; 0.05</p> <p><b>14y</b> (n=92): 0.06; 0.07</p> <p><b>Change 9-14y</b> (n=92): -0.02; 0.02</p> <p><b>Girls: kcal; % energy</b></p> <p><b>12y</b> (n=136): 0.24, <math>p &lt; 0.10</math>; <b>0.25, <math>P &lt; 0.05</math></b></p> <p><b>13y</b> (n=130): 0.16; 0.20</p> <p><b>14y</b> (n=120): 0.20; <b>0.26, <math>P &lt; 0.05</math></b></p> <p><b>Change 9-14y</b> (n=108): <b>0.35, <math>p &lt; 0.05</math>;</b> <b>0.42, <math>P &lt; 0.05</math></b></p> <p><b>Refer to paper and supplemental data for additional analyses on:</b></p> <ul style="list-style-type: none"> <li>Milk and alternatives intake</li> <li>High-fat milk and alternatives intake</li> <li>Low-fat milk and alternatives intake</li> <li>Comparison of Dietary Intake (at 9 years) Among Leaner and Heavier Twins From Discordant and Concordant MZ Twin Pairs</li> <li>Comparison of Dietary Intake at 9 Years Between Discordant MZ Twins for BMI at 9 Years and Older</li> </ul>	



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Fiorito, 2009<sup>21</sup></b>  <b>Prospective Cohort Study, United States</b>  Baseline N=197, Analytic N=166 (Attrition: 16%); Power: NR</p> <p><b>Recruitment:</b> Convenience sample via flyers, newspaper advertisements, and mailings/follow-up phone calls</p> <p><b>Participant characteristics: Girls</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 100%</li> <li>• Age: ~5y</li> <li>• Race/ethnicity: Predominantly non-Hispanic white</li> <li>• SES, Mean (SD): Family income, averaged \$50,000-\$75,000; Paternal education, 14.9y (2.7); Maternal education, 14.8y (2.3)</li> <li>• Anthropometrics, Mean (SD): BMI for age percentile, 59.3 (26.6); Body fat %, 20.6 (4.3); Overweight 18%</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Among girls, milk intake at 5y of age was not significantly associated with body fat percentage through age 15.</p>	<p><b>Exposure of interest:</b> Milk (whole and reduced fat, plain or flavored, milk consumed as a beverage); 1 svg=8oz</p> <p><b>Comparator:</b> Milk intake (continuous; 8 oz svg/d)</p> <p>Other exposures: fruit juice, sweetened beverage</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Three, 24-hr recalls (2 weekdays, 1 weekend day) within 2- to 3-wk period conducted by trained staff using NDS-R software and reported by mother; represents usual intake</li> <li>• At baseline (5y of age)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At 7, 9, 11, 13, 15y of age</li> <li>• Body fat % estimated by tricep and subscapular skinfold thickness at age 5, 7, 9, and 11y and DXA scans at age 9, 11, 13 and 15</li> </ul>	<p><b>Body fat percentage</b>, standardized regression coefficient, linear regression  7y (N=169): -0.02, P=NS  9y (N=158): -0.06, P=NS  11y (N=164): 0.01, P=NS  13y (N=150): 0.04, P=NS  15y (N=160): -0.08, P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Reporting bias: not all outcome measures reported for each beverage type</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH; The National Dairy Council</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Haines, 2007<sup>26</sup></b>  <b>Prospective Cohort Study, Project Eating Among Teens, United States</b>  Baseline N=4746, Analytic N=2516 (Attrition: 47%); Power: NR</p> <p><b>Recruitment:</b> population based sample</p> <p><b>Participant characteristics: adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean (SD): Girls, 1994 kcal/d (1047); Boys,</li> <li>Sex (female): 55.1%</li> <li>Age, Mean (SD): Middle school cohort, 12.8 y (0.8); High school cohort, 15.8y (0.8)</li> <li>Race/ethnicity: 48.3% white, 18.9% black, 19.6% Asian, 5.8% Hispanic, 3.6% Native American, 3.8% mixed race or other</li> <li>SES: Low or low-middle SES, 37%</li> <li>Anthropometrics: BMI (Mean), Girls 22.4, Boys 22.5; Overweight (&gt;85<sup>th</sup> percentile), Girls 25.7%, Boys 26.4%</li> <li>Physical activity, Mean (SD): Girls, 5.8 h/wk (4.7); Boys,</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In adolescent boys, greater baseline milk intake and greater increases in milk intake were associated with lower odds of incident overweight at 5y follow-up. In adolescent girls, milk intake was not significantly associated with overweight.</p>	<p><b>Exposure of interest:</b> Milk (skim, 1%, 2%, and whole white milk, chocolate milk)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Milk intake (continuous; svg/d) <ul style="list-style-type: none"> <li>Baseline intake</li> <li>Change in intake</li> </ul> </li> </ul> <p>Other exposures: sugar-sweetened beverages, diet soda</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>149 item semi-quantitative Youth and Adolescent FFQ (YAQ); Represents usual intake</li> <li>At baseline, 5y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk, Girls, Mean (SD): 1.4 svg/d (1.4)</li> <li>Milk, Boys, Mean (SD): 1.9 svg/d (1.5)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 5y follow-up</li> <li>Weight and height self-reported</li> <li>Overweight defined as BMI &gt;85<sup>th</sup> percentile for age and gender, using Must et al. classification</li> </ul>	<p><b>GIRLS:</b>  <b>Overweight at 5y follow-up</b>, OR (95% CI), linear regression  Baseline intake: 1.11 (0.93, 1.33)  Change in intake: Data NR, P=NS</p> <p><b>Incident overweight</b>, OR (95% CI), linear regression  Baseline intake: 1.31 (0.99, 1.73)  Change in intake: Data NR, P=NS</p> <p><b>BOYS:</b>  <b>Overweight at 5y follow-up</b>, OR (95% CI), linear regression  Baseline intake: 0.90 (0.75, 1.07)  Change in intake: Data NR, P=NS</p> <p><b>Incident overweight</b>, OR (95% CI), linear regression  Baseline intake: <b>0.77 (0.60, 0.99)</b>  Change in intake: <b>Data NR, P&lt;0.05</b></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline,</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Cohort</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 47% with no information on non-completers</li> <li>Height and weight self-reported</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  Maternal and Child Health Bureau (HHS)</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Hasnain, 2014<sup>27</sup></b>  <b>Prospective Cohort Study, Framingham Children's Study, United States</b></p> <p>Baseline N=106, Analytic N=98 (Attrition: 8%); Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~1724 kcal/d</li> <li>Sex (female): 55.1%</li> <li>Age: 3-5y</li> <li>Race/ethnicity: 100% non-Hispanic white</li> <li>SES: Maternal education &gt;college, ~34%; 100% 2-parent household</li> <li>Anthropometrics: BMI, Mean~16.1</li> <li>Physical activity: Mean~10.7 Caltrac counts/hr</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Greater milk intake from 3-9y was associated with lower body fat % and smaller sum of skinfolds at 15-17y; there was no significant association between milk intake and BMI or waist circumference.</p>	<p><b>Exposure of interest:</b> Milk (plain and flavored milk, small quantities of soy milk and rice beverages)</p> <p><b>Comparators:</b> Milk intake (categorical; tertiles)</p> <ul style="list-style-type: none"> <li>T1 (Mean=5.0 oz/d, SD=2.2)</li> <li>T2 (Mean=8.9 oz/d, SD=1.6)</li> <li>T3 (Mean=13.9 oz/d, SD=3.2)</li> </ul> <p>Other exposures: fruit and vegetable juice, SSBs, unsweetened/artificially sweetened beverages</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Up to 4 sets of 3-d diet records annually completed by parents (up to age 10y) or children (after age 10y); Represents usual intake</li> <li>At baseline (3-5y), annually for 12y (age 15-17y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Total fluid milk, Median (5<sup>th</sup>, 95<sup>th</sup> percentile): 8.8 oz/d (2.2, 15.5)</li> <li>Plain milk, Median (5<sup>th</sup>, 95<sup>th</sup> percentile): 6.9 oz/d (1.0, 14.7)</li> <li>Flavored milk, Median (5<sup>th</sup>, 95<sup>th</sup> percentile): 0.9 oz/d (0.0, 4.9)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, annually, end of follow-up (15-17y)</li> <li>Weight, height, waist circumference measured by study personnel</li> <li>Four skinfolds (triceps, subscapular, suprailiac, abdominal) measured in duplicate following standard protocol</li> <li>Percent body fat measured with DXA scan (end of follow-up only)</li> </ul>	<p><u><b>Effects of intake (by tertiles) at ages 3-9y on outcomes at end of follow-up (ages 15-17y): linear regression</b></u></p> <p><b>Body fat %</b>, Mean:  <b>T1: 30.0%, T2: Data NR, T3: 22.6%, P=0.0095</b></p> <p><b>BMI</b>, kg/m<sup>2</sup>: Data NR, P=0.0895  <b>Sum of 4 skinfolds</b>, mm: <b>Data NR, P=0.0465</b></p> <p><b>WC</b>, cm: Data NR, P=0.1318</p> <p><u><b>Effects of intake (by tertiles) on sum of skinfolds over time: mixed model</b></u></p> <p><b>T1 vs T2: P=0.0106</b>  <b>T1 vs T3: P=0.0371</b>  T2 vs T3: P=0.6859</p>	<p><b>TEI adjusted:</b> Evaluated but not independent predictor so removed from model</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Percent of calories from fat, mean TV and video time, other beverages consumed, maternal education, maternal BMI</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Validation of 3-d diet records not indicated</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NHLBI; National Dairy Council</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Huh, 2010<sup>29</sup></b>  <b>Prospective Cohort Study, Project Viva, United States</b>  Baseline N=1579, Analytic N=852  (Attrition: 54%) Power: NR</p> <p><b>Recruitment:</b> children born to Project Viva mothers</p> <p><b>Participant characteristics: toddlers</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean: ~1547 kcal/d</li> <li>Sex (female): NR</li> <li>Age, Mean: ~2y</li> <li>Race/ethnicity: 74% White, 9% Black, 17% Other</li> <li>SES: Yearly household income, 10% &lt;\$40,000, 21% \$40,000-70,000, 69% &gt;\$70,000</li> <li>Anthropometrics, Mean: BMI ~13.5, BMI z score, ~ -0.19</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In toddlers, total, reduced-fat, and 1%/nonfat milk intake at 2y of age was not associated with BMI z-score or incident overweight at 3y of age. Greater whole milk intake was associated with lower BMI z-score, but this association was not significant when only normal weight children at baseline were included.</p>	<p><b>Exposure of interest:</b> Milk (whole, reduced-fat, 1%/nonfat)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Whole milk intake (continuous; svg/d)</li> <li>Reduced-fat milk intake (continuous; svg/d)</li> <li>1%/nonfat milk intake (continuous; svg/d)</li> <li>Total milk intake (continuous; svg/d)</li> </ul> <p>Other exposures: spreads, whipping cream, low fat dairy, medium fat dairy, high fat dairy</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Semi-quantitative child FFQ previously validated in preschool children and completed by mothers; represents usual intake</li> <li>At baseline (2y of age)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Total milk, Mean (SD): 2.6 (1.2) svg/d</li> <li>Predominant milk type consumed: 53.1% whole milk, 26.5% reduced-fat milk, 20.4% 1%/nonfat milk</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (2yo), 1y follow-up (3yo)</li> <li>Height and weight measured by study personnel</li> <li>Sex and age specific BMI z score calculated using US national reference data</li> <li>Overweight defined as BMI for age and sex ≥85<sup>th</sup> percentile</li> </ul>	<p><b>Whole milk, continuous BMI z-score</b>, B (95% CI), linear regression:  <b>-0.09 (-0.16, -0.01), P=0.02</b>  <i>Among normal weight (N=645) at baseline:</i>  -0.05 (-0.13, 0.02), P=0.18  <b>Incident overweight</b>, OR (95% CI), logistic regression:  1.04 (0.74, 1.44), P=0.84</p> <p><b>Reduced-fat milk, continuous BMI z-score</b>, B (95% CI), linear regression:  -0.08 (-0.17, 0.01), P=0.07  <i>Among normal weight (N=645) at baseline:</i>  -0.08 (-0.17, 0.02), P=0.13  <b>Incident overweight</b>, OR (95% CI), logistic regression:  0.91 (0.62, 1.34), P=0.63</p> <p><b>1%/nonfat milk, continuous BMI z-score</b>, B (95% CI), linear regression:  0.05 (-0.06, 0.16), P=0.39  <i>Among normal weight (N=645) at baseline:</i>  0.00 (-0.14, 0.14), P=0.96  <b>Incident overweight</b>, OR (95% CI), logistic regression:  0.95 (0.58, 1.55), P=0.83</p> <p><b>Total, continuous BMI z-score</b>, B (95% CI), linear regression:  -0.05 (-0.10, 0.00), P=NS  <b>Incident overweight</b>, OR (95% CI), logistic regression:  1.01 (0.76, 1.15), P=NS</p>	<p>TEI adjusted: Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Nondairy beverage intake, television viewing, maternal BMI, paternal BMI</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 54%, however analyses compared included and excluded subjects</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH; Rexall Cy Pres Fund</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Kral, 2008<sup>33</sup></b>  <b>Prospective Cohort Study, United States</b>            Baseline N=NR, Analytic N=49 (Attrition: NR); Power: NR</p> <p><b>Recruitment:</b> convenience sample from newborn nurseries, obstetric practices, pediatric practices and local referrals</p> <p><b>Participant characteristics: children at high or low risk for obesity</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female) at age 3: ~44%</li> <li>• Age: Mean ~3 y</li> <li>• Race/ethnicity: 100% White</li> <li>• SES: NR</li> <li>• Anthropometrics at age 3: BMI z-score, Mean ~ -0.4; WC, Mean ~49.8 cm</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            Greater increases in milk intake from 3 to 5y was associated with lower WC, but not BMI z-score, from 5 to 6y.</p>	<p><b>Exposure of interest:</b> Milk (all milk and milk based beverages including chocolate milk, milk with powder/syrup, buttermilk, and milkshakes)</p> <p><b>Comparator:</b> Milk intake (change from 3y to 5y; continuous; kcal/d)</p> <p>Other exposures: fruit juice, fruit drinks, soda, diet soda, soft drinks including all soda and fruit drinks, soft drinks + fruit juice, all beverages</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Three day weighed food and beverage record (2 weekdays, 1 weekend day) recorded by primary caregiver; Represents usual intake</li> <li>• At baseline (3y), annually (4y and 5y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Milk: Mean ~7.5 oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, annually (4y, 5y, and 6y)</li> <li>• Waist circumference measured in triplicate at the narrowest part of torso by trained anthropometrists</li> <li>• Height and weight measured in triplicate by trained anthropometrists</li> <li>• BMI z-score calculated using CDC growth charts</li> </ul>	<p><b>BMI z-score change from 5y – 6y</b>, per change in kcal/d from 3y – 5y, B (SE), Linear mixed model:            Data NR, P&gt;0.10</p> <p><b>WC change from 5y – 6y</b>, per change in kcal/d from 3y – 5y, B (SE), Linear mixed model:  <b>Outliers excluded</b>  <b>-0.01 (0.004), P=0.04</b>  <b>Outliers included</b>            -0.01, P=0.055</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, race/ethnicity, anthropometry at baseline</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Exposure data based on parental weighed food records</li> <li>• Baseline n NR; No information to assess risk of bias due to missing data</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>            NIH; General Clinical Research Center; Nutrition Center of the Children's Hospital of Philadelphia</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Laurson, 2008<sup>37</sup></b>  <b>Prospective Cohort Study, United States</b>  Baseline N=301, Analytic N=268 (Attrition: 10.9%); Power: NR</p> <p><b>Recruitment:</b> communities in Idaho, Montana, Wyoming; details NR</p> <p><b>Participant characteristics: rural children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 46%</li> <li>Age: Mean~10.7y</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI, Mean~19.0 kg/m<sup>2</sup>; Normal weight 74%</li> <li>Physical activity: total score, Mean~85</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In boys and girls, milk intake and change in milk intake were not significantly associated with changes in BMI over 18-months.</p>	<p><b>Exposure of interest:</b> Milk intake</p> <p><b>Comparators:</b> Milk intake (continuous; svg/wk)</p> <p>Other exposure measures: SSB</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Unvalidated questionnaire, how often they consumed milk (per week); represents usual intake</li> <li>At baseline, 18mo follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk intake at baseline, Mean (SD): Boys 10.5 (4.4), Girls 9.3 (4.6)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 18mo follow-up</li> <li>Height and weight measured using standard procedures; details NR</li> <li>BMI calculated weight in kg divided by height in meters squared</li> <li>Normal weight (BMI-for-age&lt;85<sup>th</sup>%); Non-obese (BMI-for-age&lt;95<sup>th</sup>%)</li> </ul>	<p><b>BMI, 18-mo change based on baseline milk intake</b>, Linear regression, <math>\beta</math> (SE):</p> <p><b>Boys: Change per svg/wk increase:</b>  Overall sample: 0.006 (0.027), P=0.942  Normal weight: 0.016 (0.029), P=0.881  Non-obese: 0.020 (0.027), P=0.830</p> <p><b>Girls: Change per svg/wk increase:</b>  Overall sample: 0.117 (0.027), P=0.213  Normal weight: 0.017 (0.025), P=0.869  Non-obese: 0.147 (0.027), P=0.131</p> <p><b>BMI, 18-mo change based on change in milk intake</b>, Linear regression, <math>\beta</math> (SE):</p> <p><b>Boys: Change per svg/wk increase:</b>  Overall sample: 0.129 (0.26), P=0.168  Normal weight: 0.052 (0.029), P=0.671  Non-obese: 0.076 (0.025), P=0.454</p> <p><b>Girls: Change per svg/wk increase:</b>  Overall sample: 0.071 (0.031), P=0.500  Normal weight: 0.166 (0.032), P=0.180  Non-obese: 0.135 (0.033), P=0.234</p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  State of residence</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure not clearly defined; tool not validated</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  USDA</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><u>Lin, 2012</u><sup>39</sup></p> <p><b>Prospective Cohort Study, “Children of 1997” Birth Cohort, Hong Kong</b></p> <p>Baseline N=5968, Analytic N=3622 (Attrition: 39.3%); Power: NR</p> <p><b>Recruitment:</b> first postnatal visit</p> <p><b>Participant characteristics: Chinese adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 51.4%</li> <li>Age: 11y</li> <li>Race/ethnicity: Mother’s birthplace: Mainland China or elsewhere 37%, Hong Kong 63%</li> <li>SES: Highest parental education: ≤Grade 9 28%, Grade 10-11 43%, ≥Grade 12 29%</li> <li>Anthropometrics: BMIZ, Mean~0.24</li> <li>Physical activity: &lt;1 hr/d 71%, ≥1 hr/d 29%</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In Chinese adolescents, milk intake at age 11 was not significantly associated with changes in BMIZ at age 13.</p>	<p><b>Exposure of interest:</b> Milk intake (cow’s milk/milk powder)</p> <p><b>Comparator:</b> Milk intake (categorical; times/wk):</p> <ul style="list-style-type: none"> <li>None (ref)</li> <li>1-3</li> <li>4-6</li> <li>Daily</li> </ul> <p>Other exposure measures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents usual intake</li> <li>At baseline (age 11y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk intake (times/wk): None 34%, 1-3 34%, 4-6 10%, Daily 22%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 1.5y follow-up (range: 12-13.6y)</li> <li>Weight and height measured through annual check-ups from Dept of Health-Student Health Services using undisclosed methods</li> <li>Age- and sex-specific BMI z-scores (BMIZ) calculated based on 2007 WHO growth standard</li> </ul>	<p><b>BMIZ</b>, mean difference in BMIZ at 13y per milk intake at 11y; Linear regression, <math>\beta</math> (95% CI)</p> <p><b>With multiple imputation</b></p> <p>None (ref, n=2067)</p> <p>1-3 times/wk (n=2110): 0.003 (-0.04, 0.05)</p> <p>4-6 times/wk (n=555): -0.01 (-0.08, 0.06)</p> <p>Daily (n=1236): -0.01 (-0.07, 0.05)</p> <p>P for trend=0.655</p> <p><b>Available case analysis (no imputation)</b></p> <p>None (ref, n=1003)</p> <p>1-3 times (n=997): -0.02 (-0.07, 0.04)</p> <p>4-6 times (n=282): -0.05 (-0.14, 0.03)</p> <p>Daily (n=615): -0.05 (-0.12, 0.03)</p> <p>P for trend=0.128</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b></p> <p>Vegetable, fruit, and soft drink consumption, birth order, maternal age, maternal birthplace, birth weight, breastfeeding, pubertal stage, other food consumption (fish, seafood, meat, soy milk, tea, water, etc.)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>FFQ measured frequency of intake (times/wk), did not assess portions/amounts</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>Government of Hong Kong; Government of the Hong Kong SAR; University of Hong Kong</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Marabujo, 2018<sup>40</sup></b>  <b>Prospective Cohort Study, Epidemiological Health Investigation of Teenagers (EPITeen), Portugal</b>  Baseline N=2159, Analytic N=941 (Attrition: 56.4%); Power: NR</p> <p><b>Recruitment:</b> public and private schools</p> <p><b>Participant characteristics: adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean ~2438 kcal/d</li> <li>Sex (female): 53%</li> <li>Age: 13y</li> <li>Race/ethnicity: NR</li> <li>SES: Parents maximum education level: 1-4<sup>th</sup> grade 10%, 5-6<sup>th</sup> grade 9%, 7-9<sup>th</sup> grade 17%, 10-11<sup>th</sup> grade 13%, 12<sup>th</sup> grade 19%, College 33%</li> <li>Anthropometrics: Underweight/normal weight 76%, Overweight 15%, Obese 9%</li> <li>Physical activity: Extracurricular activity ≥20 min duration: Never 17%, &lt;1/wk 10%, 1/wk 12%, 2-3/wk 35%, 4-6/wk 12%, Almost daily 15%</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In adolescent girls, after adjustment for confounders, there was no association between milk intake at age 13 and BMI at age 21.</p>	<p><b>Exposure of interest:</b> Milk intake (sum of skim, semi-skimmed, and full fat milks)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Milk intake (continuous; 100 g/d)</li> <li>Milk intake (categorical; cups/d): <ul style="list-style-type: none"> <li>≤1</li> <li>2-3</li> <li>&gt;3</li> </ul> </li> </ul> <p>Other exposure measures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents usual dietary intake in previous 12 months</li> <li>At baseline (age 13), 8y follow-up (age 21)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk intake at baseline: Mean~406 g/d</li> <li>Frequency of milk intake at baseline (cups/d): ≤1: 56%; 2-3: 36%; &gt;3: 8%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (age 13), 8y follow-up (age 21)</li> <li>Height measured by trained health professionals using stadiometer</li> <li>Weight measured by trained health professionals using digital scale</li> <li>BMI calculated as weight in kg divided by height in meters squared</li> </ul>	<p><b>BMI</b>, association between milk intake at age 13 and BMI at age 21 (change per 100 g/d increase); Linear regression, <math>\beta</math> (95% CI)  TEI unadj: -0.021 (-0.107, 0.066)  TEI adj: -0.018 (-0.106, 0.069)</p> <p><b>BMI at 21y per milk intake at 13y</b>, ANOVA, Mean (SD)  <b>Full sample:</b>  ≤1 cup/d (n=527): 23.0 (4.0)  2-3 cups/d (n=342): 22.6 (3.3)  &gt;3 cups/d (n=72): 23.8 (4.4)  P=0.05</p> <p><b>Girls (n=501):</b>  ≤1 cup/d: <b>22.6 (3.9)</b>  2-3 cups/d: <b>22.1 (3.3)</b>  &gt;3 cups/d: <b>24.5 (5.2)</b>  <b>P=0.002</b></p> <p><b>Boys (n=440):</b>  ≤1 cup/d: 23.5 (4.0)  2-3 cups/d: 23.2 (3.2)  &gt;3 cups/d: 23.0 (3.1)  P=0.572</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, physical activity, smoking</li> <li>Other factors considered: total energy intake, supplements, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, anthropometry at baseline, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications</li> </ul> <p><b>Additional model adjustments:</b>  Follow-up period, total calcium intake at follow-up, self-reported diabetes, asthma and eating disorders</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 56% without information on non-completers</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  FEDER; Foundation for Science and Technology-FCT; Unidade de Investigação em Epidemiologia (EPIUnit)</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Marshall, 2018<sup>2</sup></b>  <b>Prospective Cohort Study, Iowa Fluoride and Iowa Bone Development Studies, United States</b>  Baseline N=717, Analytic N=571 (Attrition: 20.4%); Power: NR</p> <p><b>Recruitment:</b> at birth</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: at 2-4.7y, Median~1360 kcal/d</li> <li>Sex (female): 51%</li> <li>Age: Range=2-4.7y</li> <li>Race/ethnicity: Non-Hispanic white: 94%</li> <li>SES: Mother had 4y college degree: 45%, Household annual income ≥\$60,000: 19%</li> <li>Anthropometrics: Weight, Mean~20.0 kg; Height, Mean~111.4 cm</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, when controlling for energy intake, milk intake was significantly associated with increased height.</p>	<p><b>Exposure of interest:</b> Milk intake (all forms of cow's milk, including chocolate, low-fat, whole)</p> <p><b>Comparator:</b> Milk intake (continuous; 8 oz/d)</p> <p>Other exposure measures: juice, SSB, water/other sugar-free beverages</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated beverage frequency questionnaire; represents previous week's beverage intakes</li> <li>At 3- to 6-mo intervals: 2-4.7, 5-8.5, 9-10.5, 11-12.5, 13-14.5, and 15-17y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk intake at 2-4.7y: Median=10.9 oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At ages 5, 9, 11, 13, 15, 17y</li> <li>Height measured without shoes using stadiometer during clinic visits</li> </ul>	<p><u>Height</u>, cm, <b>Change per 8 oz/d increase</b>; Linear regression:  <b>B: 0.39, 95% CI: 0.18, 0.60, P&lt;0.001</b></p>	<p>TEI adjusted: Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake, protein</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No information on missing data</li> <li>Registry does not contain data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>  NIH; The Roy J. Carver Charitable Trust; Delta Dental of Iowa Foundation</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Marshall, 2019<sup>41</sup></b>  <b>Prospective Cohort Study, Iowa Fluoride and Iowa Bone Development Studies, United States</b>  Baseline N=720, Analytic N=623 (Attrition: 13.5%); Power: NR</p> <p><b>Recruitment:</b> at birth</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: at 2-4.7y, Median~1360 kcal/d</li> <li>Sex (female): 51%</li> <li>Age: Range=2-4.7y</li> <li>Race/ethnicity: Non-Hispanic white 94%</li> <li>SES: Mother had 4y college degree 45%; Household annual income ≥\$60,000 19%; Low 25%, Middle 38%, High 38%</li> <li>Anthropometrics: BMI, Mean~16.0 kg/m<sup>2</sup>; BMIZ, Mean~0.31</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, when controlling for energy intake, milk intake was not significantly associated with changes in BMIZ.</p>	<p><b>Exposure of interest:</b> Milk intake (all forms of cow's milk, including chocolate, low-fat, whole)</p> <p><b>Comparator:</b> Milk intake (continuous; 8 oz/d)</p> <p>Other exposure measures: juice, SSB, water/other sugar-free beverages</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated beverage frequency questionnaire; represents previous week's beverage intakes</li> <li>At 3- to 6-mo intervals: 2-4.7, 5-8.5, 9-10.5, 11-12.5, 13-14.5, and 15-17y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk intake at 2-4.7y: Median=10.9 oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At ages 5, 9, 11, 13, 15, 17y</li> <li>Height measured without shoes using stadiometer during clinic visits</li> <li>Weight was measured at clinic visit using a standard physician's scale</li> <li>BMIs were calculated from weight and height measures (kg/m<sup>2</sup>)</li> <li>Age- and sex-specific BMI z-scores (BMIZ) calculated 2000 CDC growth charts</li> </ul>	<p><b>BMIZ, Change per 8 oz/d increase in milk, Linear regression:</b>  B: 0.022, 95% CI: -0.007, 0.052, P=0.13</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES</li> <li>Other factors considered: total energy intake, protein</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Other beverage intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No information on missing data</li> <li>Registry does not contain data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>  NIH; The Roy J. Carver Charitable Trust; Delta Dental of Iowa Foundation</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Newby, 2004<sup>43</sup></b>  <b>Prospective Cohort Study, United States</b>            Baseline N=1450, Analytic N=1345 (Attrition: 7%); Power: NR</p> <p><b>Recruitment:</b> WIC clinic, North Dakota</p> <p><b>Participant characteristics: low-income preschool children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~1747 kcal/d</li> <li>Sex (female): 49.8%</li> <li>Age, Mean (SD): 2.9 (0.7) y</li> <li>Race/ethnicity: White 83%, Native American 11%, Other 6%</li> <li>SES: Maternal education, Mean~12.6y; Poverty level: &lt;100%: 55%; 100-133%: 22%; &gt;133-185%: 23%</li> <li>Anthropometrics: BMI, Mean~16.6 kg/m<sup>2</sup>; At risk of overweight 14%, Overweight 6%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            In low-income preschool children, when controlling for energy intake or not, milk intake was not significantly associated with changes in weight or BMI</p>	<p><b>Exposure of interest:</b> Milk intake (all types together since majority of children consumed 2% or whole milk)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Milk intake (continuous; oz/d)</li> <li>Milk intake (categorical; oz/d)               <ul style="list-style-type: none"> <li>&lt;24 (ref)</li> <li>≥24</li> </ul> </li> </ul> <p>Other exposure measures: fruit juice, fruit drinks, soda, diet soda</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents dietary intake during previous month</li> <li>At baseline, follow-up 6-12mo later (mean 8.4mo)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk intake at baseline: Mean~19.9 oz/d; ≥24 oz/d: 33%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, follow-up 6-12mo later</li> <li>Height measured by trained staff using wall-mounted measuring board</li> <li>Weight measured by trained staff using standard floor-model beam scale</li> <li>Age- and sex-specific BMI calculated based on 2000 CDC growth charts</li> <li>At risk of overweight (BMI 85<sup>th</sup> to &lt;95<sup>th</sup>%); Overweight (BMI≥95<sup>th</sup>%)</li> </ul>	<p><b>Weight</b>, Linear regression  <b>Change per oz/d increase, <math>\beta</math> (SE):</b>            TEI adj: 0.00 (0.01), P=0.84  <b>&lt;24 oz/d (ref) vs. ≥24 oz/d:</b>            P=NS, Data NR</p> <p><b>BMI</b>, Linear regression  <b>Change per oz/d increase, <math>\beta</math> (SE):</b>            TEI adj: -0.00 (0.00), P=0.96  <b>&lt;24 oz/d (ref) vs. ≥24 oz/d:</b>            P=NS, Data NR</p> <p>Estimates remained similar when TEI was omitted from model. (Data NR)</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>            Birth weight, other beverages</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Potential selection bias by only including participants with 2 WIC clinic visits 6-12 months apart</li> <li>No preregistered data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>            USDA; NIH Health Harvard Education Program in Cancer Prevention Control; Boston Obesity Nutrition Research Center</p>

Noel, 2011<sup>44</sup>

**Prospective Cohort Study, Avon Longitudinal Study of Parents and Children (ALSPAC), United Kingdom**

Baseline N=14,536 (recruited), Analytic N=2245 (Attrition: 85%); Power:  $\beta > 80\%$  to detect associations between milk intakes and BF% of 0.003 at age 11y and 0.003 at age 13y,  $\alpha = 0.05$

**Recruitment:** pregnant women through media campaign and routine maternity visit

**Participant characteristics: children**

- Total energy intake: NR
- Sex (female): 55%
- Age, y, Mean (SD): 10.6 (0.22)
- Race/ethnicity: "limited variability in race/ethnicity"
- SES: Mother's educational attainment: CSE/vocational 16%, Ordinary level 36%, Advanced level/degree 48%
- Anthropometrics: Body weight, Mean~37.5 kg; Height, Mean~144 cm; Body fat, Mean~25.5%
- Physical activity: Mean~588 counts/min
- Smoking: NR

**Summary of findings:**

In children, when controlling for total energy intake, total milk intake was significantly associated with decreased BF% at 1y follow-up, but not at 3y follow-up. When energy intake was not controlled for, this association was not significant. There was no significant association between BF% and plain milk, full-fat milk, or reduced-fat milk at 1y or 3y follow-up.

**Exposure of interest:** Milk intake (full-fat, reduced-fat, nonfat, flavored cow's milk); 1 svg = 8-oz of milk (244 g regular milk and 250 g flavored milk)

**Comparators:** Milk intake (continuous; svg/d)

Other exposure measures: none

**Exposure assessment method and timing:**

- 3-d dietary record completed by child with parental assistance as needed; represents dietary intake on both weekdays and weekend
- Plausible dietary reporters based on previously published age- and sex-specific cutoffs
- At baseline (age 10y), 3y follow-up (age 13y)

**Study beverage intake:**

- Total milk intake (svg/d), Mean (SD): Boys 1.04 (0.78), Girls 0.79 (0.67)
- Full-fat milk intake (svg/d), Mean (SD): Boys 0.36 (0.67), Girls 0.26 (0.52)
- Reduced-fat milk intake (svg/d), Mean (SD): Boys 0.65 (0.75), Girls 0.50 (0.63)

**Outcome assessment methods/timing:**

- At 1y (age 11y) and 3y follow-up (age 13y)
- Body fat percentage (BF%) determined using DEXA
- Height measured using stadiometer
- Weight measured using scale
- BMI calculated

**BF%,  $\beta$  (95% CI), Linear regression**

Total Milk (plain milk and flavored milk)

**Change at 1y f/u (age 11):**

**Per 100 g milk consumed:**

**TEI adj: -0.14 (-0.26, -0.01), P=0.03**

TEI unadj: 0.01 (-0.18, 0.20), P=0.89; plausible reporters (n=907): -0.16 (-0.37, 0.06), P=0.16

**Per milk svg/d:**

**TEI adj: -0.34 (-0.64, -0.03), P=0.03**

TEI unadj: 0.03 (-0.44, 0.50), P=0.89; plausible reporters (n=907): -0.38 (-0.91, 0.15), P=0.16

**Change at 3y f/u (age 13):**

**Per 100 g milk consumed:**

TEI adj: -0.06 (-0.21, 0.09), P=0.45

TEI unadj: 0.03 (-0.22, 0.27), P=0.83; plausible reporters (n=876): -0.20 (-0.43, 0.03), P=0.10

**Per milk svg/d:**

TEI adj: -0.15 (-0.52, 0.23), P=0.45

TEI unadj: 0.06 (-0.53, 0.65), P=0.83; plausible reporters (n=876): -0.49 (-1.06, 0.09), P=0.10

*Plain Milk (full-fat, reduced-fat, nonfat)*

"Associations between plain milk intake and BF% for all models were similar to those observed with total milk intake (Data NR)"

*Full-fat Milk*

**Change at 1y f/u per 100 g milk**

**consumed:**

TEI adj: -0.10 (-0.24, 0.05), P=0.19

TEI unadj: -0.03 (-0.18, 0.12), P=0.70; plausible reporters (n=907): -0.04 (-0.32, 0.24), P=0.80

**Change at 1y f/u per milk svg/d:**

TEI adj: -0.24 (-0.60, 0.12), P=0.19

TEI unadj: -0.07 (-0.44, 0.29), P=0.70; plausible reporters (n=907): -0.09 (-0.77, 0.59), P=0.80

**Change at 3y f/u per 100 g milk**

**consumed:**

TEI adj: -0.10 (0.28, 0.08), P=0.28

**TEI adjusted:** Yes and No

**Confounders accounted for:**

- Key confounders: sex, age, SES, anthropometry at baseline, physical activity
- Other factors considered: total energy intake

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity, smoking
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:** Pubertal status, maternal BMI, dietary intake (total fat, ready-to-eat breakfast cereal, 100% fruit juice, SSB, calcium intake)

**Limitations:**

- Not all key confounders accounted for
- Baseline n not clear
- Did not report all outcomes assessed (height, weight, BMI)
- No preregistered data analysis plan

**Funding sources:**

American Diabetes Association; UK Medical Research Council; Wellcome Trust; University of Bristol; NHLBI; Arthritic Association

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
		<p>TEI unadj: -0.06 (-0.24, 0.13), P=0.56;  plausible reporters (n=876): -0.21 (-0.48, 0.07), P=0.14</p> <p><b>Change at 3y f/u per milk svg/d:</b>  TEI adj: -0.24 (-0.69, 0.20), P=0.28  TEI unadj: -0.14 (-0.59, 0.32), P=0.56;  plausible reporters (n=876): -0.50 (-1.17, 0.17), P=0.14</p> <p><i>Reduced-fat Milk</i>  <b>Change at 1y f/u per 100 g milk consumed:</b>  TEI adj: -0.05 (-0.17, 0.08), P=0.47  TEI unadj: 0.07 (-0.08, 0.22), P=0.36;  plausible reporters (n=907): -0.09 (-0.30, 0.13), P=0.44</p> <p><b>Change at 1y f/u per milk svg/d:</b>  TEI adj: -0.11 (-0.41, 0.19), P=0.47  TEI unadj: 0.17 (-0.19, 0.54), P=0.36;  plausible reporters (n=907): -0.21 (-0.73, 0.32), P=0.44</p> <p><b>Change at 3y f/u per 100 g milk consumed:</b>  TEI adj: 0.03 (-0.13, 0.18), P=0.74  TEI unadj: 0.09 (-0.10, 0.28), P=0.34;  plausible reporters (n=876): -0.03 (-0.27, 0.20), P=0.78</p> <p><b>Change at 3y f/u per milk svg/d:</b>  TEI adj: 0.06 (-0.32, 0.44), P=0.74  TEI unadj: 0.22 (-0.24, 0.68), P=0.34;  plausible reporters (n=876): -0.08 (-0.66, 0.50), P=0.78</p> <p><i>Skim Milk</i>  Was not examined separately since it was consumed by a small number of children (n=200 at age 10y)</p>	

Noel, 2013<sup>45</sup>

**Prospective Cohort Study, Avon Longitudinal Study of Parents and Children (ALSPAC), United Kingdom**

Baseline N=5533, Analytic N=2270  
(Attrition: 59.0%); Power: NR

**Recruitment:** pregnant women through media campaign and routine maternity visit

**Participant characteristics: normal and overweight children**

- Total energy intake: Mean~1932 kcal/d
- Sex (female): 55%
- Age: Mean~10.6y
- Race/ethnicity: "limited variability"
- SES: Maternal education: CSE/vocational 16%, Ordinary level 36%, Advanced level/degree 48%
- Anthropometrics: BMI: Overweight/Obese 21%; Body fat, Mean~25.5%
- Physical activity: Mean~588 counts/min
- Smoking: NR

**Summary of findings:**

In overweight/obese children, consuming flavored milk at age 10 was significantly associated with smaller reductions in body fat and greater weight gain at age 13 compared with non-consumers. For normal weight children, there was no significant association between flavored milk intake at age 10 and body fat or weight at age 13 compared to children who did not drink flavored milk.

**Exposure of interest:** Flavored milk intake (250 g = 1 svg)

**Comparators:** No flavored milk intake

Other exposure measures: none

**Exposure assessment method and timing:**

- 3-d dietary record completed by child with parental assistance as needed; represents dietary intake on both weekdays and weekend
- Plausible dietary reporters based on previously published age- and sex-specific cutoffs
- At baseline (age 10y), 3y follow-up (age 13y)

**Study beverage intake:**

- Flavored milk: Consumers, n=380 (16.7%), Non-consumers, n= 1890 (83.3%)
- Frequency of flavored milk intake: 1 svg/d= 50 children (2.2%), >1.5 svg/d: 11 children (0.5%)
- Flavored milk intake (g/d) of consumers, mean (SE): 142 (102)

**Outcome assessment methods/timing:**

- At baseline (age 10y), 1y (age 11y), and 3y follow-up (age 13y)
- Body fat determined using DEXA
- Height measured using stadiometer
- Weight measured using scale
- BMI percentiles calculated from 2000 CDC growth charts;
- Normal weight (BMI 5<sup>th</sup> to <85<sup>th</sup>%), Overweight/obese (BMI≥85<sup>th</sup>%)

**Body Fat**, Mean (95% CI), Linear regression

**Normal weight (n=1715)**

Flavored milk consumers vs Non-consumers: -0.70 (-1.57, 0.17) vs -0.98 (-1.71, -0.25), P=0.36 (TEI unadj)  
TEI adj: P=NS, Data NR

**Normal weight, plausible reporters (n=708)**

Flavored milk consumers vs Non-consumers: -1.35 (-2.77, 0.07) vs -1.33 (-2.54, -0.12), P=0.96 (TEI unadj)  
TEI adj: P=NS, Data NR

**Overweight/obese (n=449)**

Flavored milk consumers vs Non-consumers: **-0.79 (-2.46, 0.88) vs -2.19 (-3.60, -0.78), P=0.02** (TEI unadj)  
**TEI adj: P <0.05, Data NR**

**Overweight/obese, plausible (n=138)**

Flavored milk consumers vs Non-consumers: **-0.16 (-3.84, 3.52) vs -3.43 (-6.45, -0.42), P=0.02** (TEI unadj)  
**TEI adj: P<0.05, Data NR**

**Weight**, Mean (95% CI), Linear regres.

**Normal weight (n=1715)**

Flavored milk consumers vs Non-consumers: 11.3 (10.7, 12.0) vs 11.1 (10.6, 11.6), P=0.35 (TEI unadj)  
TEI adj: P=NS, Data NR

**Normal weight, plausible reporters (n=708)**

Flavored milk consumers vs Non-consumers: 11.1 (10.0, 12.1) vs 11.1 (10.3, 12.0), P=0.83 (TEI unadj)  
TEI adj: P=NS, Data NR

**Overweight/obese (n=449)**

Flavored milk consumers vs Non-consumers: 12.6 (10.7, 14.4) vs 11.7 (10.1, 13.2), P=0.18 (TEI unadj)  
TEI adj: P=NS, Data NR

**Overweight/obese, plausible (n=138)**

Flavored milk consumers vs Non-consumers: **14.5 (11.1, 18.0) vs 11.6 (8.8, 14.4), P=0.02** (TEI unadj)  
**TEI adj: P<0.05, Data NR**

**TEI adjusted:** Yes and No

**Confounders accounted for:**

- Key confounders: sex, age, SES, anthropometry at baseline, physical activity
- Other factors considered: total energy intake, fiber

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity, smoking
- Other factors considered: timing, temporal use, sugar, protein, energy density, medications, supplements, alcohol

**Additional model adjustments:** Pubertal status, maternal BMI, dietary intake (total fat, ready-to-eat cereal, fruit, vegetables, 100% fruit juice, SSB, plain milk), calcium, dieting at age 13

**Limitations:**

- Not all key confounders accounted for
- No information on missing data
- No preregistered data analysis plan

**Funding sources:**

American Diabetes Association; UK Medical Research Council; Wellcome Trust; University of Bristol; NHLBI

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Scharf, 2013<sup>51</sup></b>  <b>Prospective Cohort Study, Early Childhood Longitudinal Survey Birth Cohort, United States</b>  Baseline N=10,700, Analytic N=8,100 (Attrition: 24.3%); Power: NR</p> <p><b>Recruitment:</b> random sampling birth certificates</p> <p><b>Participant characteristics: preschool-aged children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49%</li> <li>Age: 2y</li> <li>Race/ethnicity: White 43.1%, Black 15.0%, Hispanic 20.5%, Asian 10.2%, Other 11.2%</li> <li>SES: High 16.2%, Medium high 17.6%, Medium 18.1%, Medium low 18.3%, Low 21.3%</li> <li>Anthropometrics: Normal weight 69.9%, Overweight 15.0%, Obese 15.1%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In preschool-aged children, compared to 2%/whole milk intake, skim milk intake at age 2y was significantly associated with increased odds of overweight and obesity at age 4.</p>	<p><b>Exposure of interest:</b> Milk intake (whole, 2%, 1%, skim)</p> <p><b>Comparator:</b> Milk intake (categorical; skim/1% vs 2%/whole)</p> <p>Other exposure measures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Interview with primary caregiver in the home regarding intake; represents usual weekly intake</li> <li>Baseline, 2y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Whole or 2% milk: 86% drank at baseline</li> <li>1% milk: 8.5% drank at baseline</li> <li>Skim milk: 2.1% drank at baseline</li> <li>Milk intake at 2y follow up (svg/d): &lt;2 28.5%, 2 30.8%, &gt;2 40.8%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>Baseline, 2y follow-up</li> <li>Height measured twice by trained researchers using stadiometer</li> <li>Weight measured twice by trained researchers using digital scale</li> <li>BMI calculated as weight in kilograms divided by height in meters squared</li> <li>Age- and gender-specific z-scores (BMIZ) calculated using CDC growth charts</li> <li>Weight categories: normal weight &lt;85<sup>th</sup>%, overweight &gt;85-95<sup>th</sup>%, obese &gt;95<sup>th</sup>%)</li> </ul>	<p><b>Overweight at age 4y</b>, Logistic regression, OR (95% CI)  2%/whole at age 2y (ref)  <b>1%/skim at age 2y: 1.63 (1.23, 1.86), P&lt;0.0001</b></p> <p><b>Obese at age 4y</b>, Logistic regression  2%/whole at age 2y (ref)  <b>1%/skim at age 2y: 1.65 (1.31, 2.06), P&lt;0.0001</b></p> <p><b>Change in BMIZ age 2y-4y</b>, Linear regression  2%/whole at age 2y &amp; 4y (n=4900)  1%/skim at age 2y &amp; 4y (n=250)  P=0.6</p> <p><b>Change in raw BMI age 2y-4y</b>, Linear regression  2%/whole at age 2y &amp; 4y (n=4900)  1%/skim at age 2y &amp; 4y (n=250)  P=NS, data not shown</p> <p><b>Becoming Overweight/Obese at age 4y</b>, Logistic regression  2%/whole at age 2y &amp; 4y (ref, n=4900):  1%/skim at age 2y &amp; 4y (n=250)  <b>1.57 (1.03, 2.42), P=0.04</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Juice and SSB intake, number of daily glasses of milk, maternal BMI</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Serious risk of bias in classification of exposures</li> </ul> <p><b>Funding sources:</b>  NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Striegel-Moore, 2006<sup>55*</sup></b>  <b>Prospective Cohort Study, NHLBI Growth and Health Study, United States</b></p> <p>Baseline N=2379, Analytic N=2371 (Attrition: 0.3%); Power: n=1150 per group at 90% power to detect compare change in subscapular skinfold between Black and White girls</p> <p><b>Recruitment:</b> public and parochial schools, local health maintenance organization and Girl Scout troops</p> <p><b>Participant characteristics: adolescent girls</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 100%</li> <li>• Age: Mean ~10y</li> <li>• Race/ethnicity: Black 51%, White 49%</li> <li>• SES: &lt;\$10K: 17%; \$10&lt;20K: 14%; \$20&lt;30K: 15%; \$30&lt;40K: 14%; \$40&lt;50K: 12%; \$50&lt;75K: 17%; ≥\$75K: 6%</li> <li>• Anthropometrics: Weight: ~ 37kg; Height: ~141 cm</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In adolescent girls, milk intake was not significantly associated with changes in BMI at 10y follow-up.</p> <p>* Some info on baseline data and methodology from: Obesity and CVD risk factors in black and white girls: the NHLBI Growth and Health Study. Am J Public Health. 1992; 82:1613-1620.</p>	<p><b>Exposure of interest:</b> Milk intake (whole, low-fat, skim, non-fat dry milk from powder, buttermilk, chocolate milk or cocoa, evaporated milk, milkshakes)</p> <p><b>Comparator:</b> Milk intake (continuous; 100 g/d)</p> <p>Other exposure measures: regular soda, diet soda, fruit juice, fruit drinks, coffee/tea</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated 3-d food records; represents usual intake over 3 consecutive days (2 weekdays and 1 weekend day)</li> <li>• At baseline, and annually for years 1-5, then at years 7, 8, 10</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Milk intake, g/d, Mean (SE): White, 352.04 (7.22); Black, 244.13 (5.36)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• Baseline, annually until 10y follow-up</li> <li>• Weight measured twice by research staff using electronic scale</li> <li>• Height measured twice by research staff using stadiometer</li> <li>• BMI calculated as weight in kilograms divided by height in meters squared</li> </ul>	<p><b>BMI</b>, Linear regression  <b>Change per 100g/d increase:</b>  B: -0.002, SE: 0.006, P&gt;0.05</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Consumption of other beverage types, site</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Missing data not clearly reported</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NHLBI</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Whetstone, 2012<sup>59</sup></b>  <b>Prospective Cohort Study, North Carolina Health and Wellness Trust Fund programs (NRCT), United States</b>  Baseline N=2487, Analytic N=1144 (Attrition: 54%); Power: NR</p> <p><b>Recruitment:</b> community-originated local program</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 51.7%</li> <li>• Age, mean (SD): 9.5 (4.1) y, Range: 4.1-18.6</li> <li>• Race/ethnicity: Caucasian 64.7%, African-American 35.3%, Hispanic/Latino origin 2.6%</li> <li>• SES: NR</li> <li>• Anthropometrics, mean (SD): BMI z-score: 0.82 (1.13); Weight status: underweight=1.6%, healthy weight=55.0%, overweight=16.9%, obese=26.6%</li> <li>• Physical activity: mean number of days of exercise or physical activity per week: 4.49</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Among children with overweight/obesity, those who changed from whole milk to low-fat milk improved their weight status compared to those who did not change to lower fat milk. Milk intake was not significantly associated with changes in BMIZ.</p>	<p><b>Exposure of interest:</b> Change in milk intake (from whole milk to low-fat milk)</p> <p><b>Comparator:</b> No change in milk intake</p> <p>Other exposure measures: soda</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Unvalidated health survey completed by parents (if child was grade K-5) or self (if child was grade 6-12); represents typical daily consumption</li> <li>• At baseline and every 6 months during follow-up period; average follow-up 20.5y (range: 8-29mo)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Whole milk intake at baseline: 43.6%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline and every 6 months during follow-up period; average follow-up 20.5mo (range: 8-29mo)</li> <li>• Height measured by trained staff, stadiometers recommended but alternative instructions for triangular ruler and metal tape measure provided</li> <li>• Weight measured by trained staff using balance beam or digital scale</li> <li>• BMI z-score (BMIZ) calculated using approach on CDC website</li> <li>• Weight status were age- and gender-specific CDC designations: underweight (BMI&lt;5%), healthy weight (5%≤BMI&lt;85%), overweight (85%≤BMI&lt;95%), obese (BMI≥95%)</li> </ul>	<p><b>Weight Status</b>, Percentage of <i>overweight/obese children</i> who lowered their weight status category (subgroup n NR), Chi-square difference  <b>Did not change to lower fat milk vs Changed to lower fat milk: 17.9% vs 39.6%, P=0.003</b></p> <p><b>BMIZ</b>, Change in BMIZ among <i>overweight/obese children</i> (subgroup n NR), ANOVA  Did not change to lower fat milk vs Changed to lower fat milk: -0.08 vs -0.22, P&gt;0.05</p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, anthropometry at baseline</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Grantee</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Participants hand-selected by grantee to be “representative”</li> <li>• Exposure not clearly defined; tool not validated</li> <li>• Subgroup analyses reported; Results from full sample NR; no preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  North Carolina Health and Wellness Trust Fund Commission</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Zheng, 2015<sup>1</sup></b>  <b>Prospective Cohort Study, Childhood Asthma Prevention Study (RCT), Australia</b>  Baseline N=237, Analytic N=158 (Attrition: 33.3%); Power: NR</p> <p><b>Recruitment:</b> pregnant women from antenatal clinics</p> <p><b>Participant characteristics: 8yo children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean ~8.0 MJ/d</li> <li>Sex (female): 48%</li> <li>Age: Mean ~8.0y</li> <li>Race/ethnicity: Mother born in Australia/New Zealand ~78%; Father born in Australia/New Zealand ~73%</li> <li>SES: Maternal education level &gt;12y ~55%; Paternal education level &gt;12y ~58%; Living in disadvantaged area ~20%</li> <li>Anthropometrics: BMI z-score, Mean (SD): 0.4(1.0); Overweight/obese: 27.2%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> <li>Intervention group: 54.9%</li> </ul> <p><b>Summary of findings:</b>  In children, milk consumption was not significantly associated with changes in BMIZ or %BF. Using a substitution model, substituting SSBs with milk was not significantly associated with changes in BMIZ or %BF.</p>	<p><b>Exposure of interest:</b> Milk intake (full fat, reduced fat, skim, and flavored)</p> <p><b>Comparator:</b> Milk intake (100 g/d) modeled continuously</p> <p>Other exposure measures: water, SSB, 100% fruit juice, diet drinks, and liquid energy (energy from all beverages)</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Three 24-hr dietary recalls via phone using multiple pass approach completed by children with parental assistance; Represents usual dietary intake on nonconsecutive weekdays and weekends</li> <li>At 1y follow-up (age 9y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk intake at baseline (g/d), Mean (SD): ~280(151)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>Baseline (age 8y), and 3.5y follow-up (age 11.5y)</li> <li>Weight measured to nearest 0.1kg</li> <li>Height measured using stadiometer</li> <li>Age- and sex-specific BMI z-scores (BMIZ) calculated using 2000 CDC growth charts</li> <li>Percentage body fat (%BF) measured by bioimpedance analysis</li> </ul>	<p><b>BMIZ</b>, Linear regression  <b>Change per 100 g/d increase, <math>\beta</math> (SE):</b>  TEI unadj: 0.01 (0.03), P=0.79  TEI adj: 0.05 (0.03), P=0.16</p> <p><b>%BF</b>, Linear regression  <b>Change per 100 g/d increase, <math>\beta</math> (SE):</b>  TEI unadj: 0.12 (0.29), P=0.68  TEI adj: 0.37 (0.31), P=0.24</p>	<p><b>TEI adjusted:</b> Yes and no</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Maternal age at birth, presence of gestational diabetes, exclusive breastfeeding at 3mo, pubertal status, randomization group (omega-3 fatty acid dietary supplementation and house dust mite reduction); Substitution model: EI from non-bev sources</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Anthropometric measures not taken at same time as dietary data</li> <li>Exposure data collected at 1 time to represent 3.5y period</li> </ul> <p><b>Funding sources:</b>  National Health and Medical Research Council of Australia; Cooperative Research Centre for Asthma; New South Wales Department of Health; Children's Hospital Westmead</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Zheng, 2015<sup>62</sup></b>  <b>Prospective Cohort Study, Healthy Start Study (RCT), Denmark</b>  Baseline N=552, Analytic N=352 (Attrition: 36.2%); Power: NR</p> <p><b>Recruitment:</b> Danish National Birth Register</p> <p><b>Participant characteristics: normal weight children at high-risk of overweight</b></p> <ul style="list-style-type: none"> <li>• Total energy intake, MJ/d, Mean (SD): 4.97 (0.95)</li> <li>• Sex (female): 45.2%</li> <li>• Age: 4.1 (1.1) y</li> <li>• Race/ethnicity: NR</li> <li>• SES: Maternal education level, Tertiary or above: 78.0%; Paternal education level, Tertiary or above: 61.0%; Parents divorced 5.6%</li> <li>• Anthropometrics: Mean (SD), Body weight (kg): 18.0 (3.3); BMI z-score: 0.3 (0.9)</li> <li>• Physical activity: High 59.2%</li> <li>• Smoking: NR</li> <li>• Intervention group: 46.0%</li> </ul> <p><b>Summary of findings:</b>  In children, when controlling for energy intake, milk intake was not significantly associated with changes in BMIZ and body weight. Substitution of sugary drinks with milk was associated with decreased BMIZ and body weight.</p>	<p><b>Exposure of interest:</b> Milk intake (skimmed, low-fat, whole, buttermilk, flavored)</p> <p><b>Comparator:</b> Milk intake (100g/d) modeled continuously</p> <p>Other exposure measures: water, sugary drinks, diet drinks</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• 4-d dietary record completed by parents; represents dietary intake on both weekdays and weekends</li> <li>• At baseline, 1.5y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Milk intake at baseline (g/d), Mean (SD): 259.6 (167.5)</li> </ul> <p><b>Outcomes assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 1.5y follow-up</li> <li>• Height measured using stature meter</li> <li>• Weight measured using mechanical weight or beam-scale</li> <li>• Age- and sex-specific BMI z-scores (BMIZ) calculated using Lambda-Mu-Sigma method</li> </ul>	<p><i>Nutrient Residual Model</i> (includes beverage intake residuals and total energy intake)  <b>BMIZ</b>, Linear regression  <b>Change per 100 g/d increase:</b>  B: -0.02, SE: 0.02, P=0.41</p> <p><b>Body weight</b>, Linear regression  <b>Change per 100 g/d increase:</b>  B: -0.07, SE: 0.05, P=0.13</p> <p><i>Energy Partition Model</i> (includes absolute amount of individual beverage intake and energy from non-beverage sources)  <b>BMIZ</b>, Linear regression  <b>Change per 100 g/d increase:</b>  B: -0.01, SE: 0.02, P=0.66</p> <p><b>Body weight</b>, Linear regression  <b>Change per 100 g/d increase:</b>  B: -0.07, SE: 0.04, P=0.20</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, SES, anthropometry at baseline, physical activity</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Intervention allocation, parents divorced, number of siblings living with the child, maternal pre-pregnancy overweight</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Attrition 36% without information on non-completers</li> <li>• No preregister analysis plan</li> </ul> <p><b>Funding sources:</b>  None</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Zheng, 2015<sup>61</sup></b>  <b>Prospective Cohort Study, European Youth Heart Study (EYHS), Denmark</b>  Baseline N=590, Analytic N=358 (Attrition: 39%); Power: NR</p> <p><b>Recruitment:</b> schools in Odense, Denmark</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: 9.1 (2.3) MJ/d</li> <li>Sex (female): 56%</li> <li>Age: 9.6 (0.4) y</li> <li>Race/ethnicity: NR</li> <li>SES: 47% Low (elementary, high school, or vocational education)</li> <li>Anthropometrics: BMI 17.2 (2.3) kg/m<sup>2</sup>; BMI z-score 0.4 (1.1)</li> <li>Physical activity: 55% Active (regular exercise)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In Danish children, milk intake at 9y was not significantly associated with changes in BMI, waist circumference, or skinfold measurements from age 9-15y.</p>	<p><b>Exposure of interest:</b> Milk intake (regular, low-fat, skim, plain, or flavored)</p> <p><b>Comparator:</b> Milk intake (100g/d) modeled continuously</p> <p>Other exposure measures: water, SSB, fruit juice, coffee/tea</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>One 24h recall face-to-face interview supplemented with parent-assisted food record; represents food intake</li> <li>At baseline (age 9)</li> </ul> <p><b>Study beverage intake:</b> g/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>Milk intake: 481.2 (290.9)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (age 9), and 6y follow-up (age 15)</li> <li>Height measured bare feet to nearest 5mm using stadiometer</li> <li>Weight measured to nearest 0.1 kg using beam balance scale</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>Age- and sex-specific BMI z-score (BMIZ) generated using the least mean squares method</li> <li>Waist circumference (WC) measured twice with metal anthropometric tape (mean was used)</li> <li>Sum of 4 skinfolds (<math>\Sigma 4SF</math>) obtained by adding average skinfolds of 4 sites (biceps, triceps, subscapular, and suprailiac) that were measured in duplicate with Harpenden fat calipers</li> </ul>	<p><i>Base Model</i> (Model 1 in paper) adjusted for confounders listed to the right, but did not adjust for TEI</p> <p><i>Standard Multivariate Model</i> (Model 2 in paper) adjusted for TEI</p> <p><i>Energy Partition Model</i> (Model 3 in paper) included energy-containing beverages only (ie, excluded water) and adjusted for energy from non-beverage sources.</p> <p><b>Change in BMI age 9-15y:</b> kg/m<sup>2</sup>, Per 100 g/d increase, Linear regression, <math>\beta</math> (SE), n=314  Base Model: -0.003 (0.01), P=0.79  TEI Model: -0.001 (0.01), P=0.95  Energy Partition: -0.003 (0.01), P=0.81</p> <p><b>Change in WC age 9-15y:</b> Per 100 g/d increase, Linear regression, <math>\beta</math> (SE), n=314  Base Model: -0.13 (0.11), P=0.22  TEI Model: -0.05 (0.12), P=0.65  Energy Partition: -0.09 (0.11), P=0.41</p> <p><b>Change in <math>\Sigma 4SF</math> age 9-15y:</b> mm, Per 100 g/d increase, Linear regression, <math>\beta</math> (SE), n=308  Base Model: 0.04 (0.26), P=0.87  TEI Model: 0.12 (0.29), P=0.67  Energy Partition: 0.09 (0.26), P=0.74</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Pubertal status, Sex x SES, individual beverage intakes, energy from non-beverage sources</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure only measured once (at baseline)</li> <li>Exposure measured with single 24h dietary recall—may not reflect habitual intake</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NR</p>

**Table 2. Risk of bias for randomized controlled trials examining milk consumption and growth, size, body composition and risk of overweight and obesity in children<sup>vi, vii</sup>**

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Arnberg, 2012 <sup>3</sup>	Low	Low	Low	Low	Low
Larnkjaer, 2014 <sup>35</sup>	Low	Low	Low	Low	Low
Larnkjaer, 2015 <sup>36</sup>	Low	Low	Low	Low	Low
Lambourne, 2013 <sup>34</sup>	Some Concerns	Low	Low	Low	Some Concerns

<sup>vi</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>vii</sup> Possible ratings of low, some concerns, or high determined using the "[Cochrane Risk-of-bias 2.0](#)" (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). *Cochrane Methods. Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). [dx.doi.org/10.1002/14651858.CD201601](https://doi.org/10.1002/14651858.CD201601).)

**Table 3. Risk of bias for prospective cohort studies examining milk consumption and growth, size, body composition and risk of overweight and obesity in children<sup>viii, ix</sup>**

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Berkey, 2004 <sup>7</sup>	Serious	Low	Low	Low	Moderate	Moderate	Serious
Berkey, 2005 <sup>8</sup>	Serious	Low	Low	Low	Moderate	Moderate	Moderate
Berkey, 2009 <sup>6</sup>	Serious	Low	Low	Low	Low	Moderate	Moderate
Blum, 2005 <sup>11</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
DeBoer, 2015 <sup>14</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Dong, 2015 <sup>15</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Dubois, 2016 <sup>17</sup>	Serious	Low	Low	Low	Moderate	Moderate	Moderate
Fiorito, 2009 <sup>21</sup>	Serious	Low	Low	Low	Low	Low	Serious
Haines, 2007 <sup>26</sup>	Serious	Low	Low	Low	Moderate	Moderate	Moderate
Hasnain, 2014 <sup>27</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Huh, 2010 <sup>29</sup>	Serious	Low	Low	Low	Low	Low	Moderate
Kral, 2008 <sup>33</sup>	Serious	Low	Moderate	Low	No information	Low	Moderate
Laurson, 2008 <sup>37</sup>	Serious	Low	Serious	Low	Low	Low	Moderate
Lin, 2012 <sup>39</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Marabujo, 2008 <sup>40</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Marshall, 2018 <sup>2</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Marshall, 2019 <sup>41</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Newby, 2004 <sup>43</sup>	Serious	Moderate	Low	Low	Low	Low	Moderate
Noel, 2011 <sup>44</sup>	Serious	Low	Moderate	Low	No information	Low	Moderate

<sup>viii</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>ix</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

Noel, 2013 <sup>45</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Scharf, 2013 <sup>51</sup>	Serious	Moderate	Moderate	Moderate	Moderate	Low	Moderate
Striegel-Moore, 2006 <sup>55</sup>	Serious	Low	Low	Low	No information	Low	Moderate
Whetstone, 2012 <sup>59</sup>	Serious	Critical	Serious	Low	Moderate	Moderate	Serious
Zheng, 2015 <sup>1</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Zheng, 2015 <sup>62</sup>	Serious	Low	Serious	Moderate	Serious	Low	Moderate
Zheng, 2015 <sup>61</sup>	Serious	Low	Moderate	Moderate	Low	Low	Moderate

**Table 4: Summary of articles examining the relationship between milk consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>x</sup>**

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
RANDOMIZED CONTROLLED TRIALS			

<sup>x</sup> Abbreviations: ANOVA: analysis of variance; BMI: body mass index; CI: confidence interval; d: day(s); DXA or DEXA: dual-energy X-ray absorptiometry; FFQ: food frequency questionnaire; HC: hip circumference; HR: hazard ratio; IQR: interquartile range; mo: month(s); NHLBI: National Heart, Lung, and Blood Institute; NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases; NIH: National Institutes of Health; NA: not applicable; NR: not reported; NS: not significant; OR: odds ratio; Q: quartile; RCT: randomized controlled trial; SD: standard deviation; SE: standard error; SES: socioeconomic status; SSB: sugar-sweetened beverage; T: tertile; TEI: total energy intake; USDA: U.S. Department of Agriculture; WC: waist circumference; WHO: World Health Organization; WHR: waist-to-hip ratio; wk: week(s); y: year(s)  
Red and green font indicate significant findings.

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Barr, 2000<sup>5</sup></b>  <b>RCT, United States</b>            Baseline N=204, Analytic N=200 (Attrition: 2%); Power: n=105/group, to detect 1.3 kg difference with 5% dropout, B=0.80, <math>\alpha=0.05</math></p> <p><b>Recruitment:</b> through local advertisements and outpatient clinics</p> <p><b>Participant characteristics: Adults <math>\geq 55</math>y</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean ~1683 kcal/d</li> <li>Sex (female): 65%</li> <li>Age: Mean ~65 y</li> <li>Race/ethnicity: White, 95%</li> <li>SES: Education, Mean ~15y</li> <li>Anthropometrics: BMI, Mean ~25.9</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            In older adults, increasing skim and 1% milk intake by three 8-oz servings/d led to more weight gain over 12 wk compared to a control group who maintained usual dairy intake of &lt;1.5 servings/d.</p>	<p><b>Intervention:</b> Skim and 1% milk, add three 8-oz svg/d; Women, n=63; Men, n=35</p> <p><b>Comparator:</b> Control: maintain usual intake (<math>\leq 1.5</math> dairy svg/d); Women, n=66; Men, n=36</p> <p>Other interventions: none</p> <p><u>Intervention duration:</u> 12 wk</p> <p><u>Intervention compliance:</u> daily milk intake logs collected at 4, 8, 12 wk; Glasses/d at: wk 4, women 2.90, men 3.14; wk 8, women 2.89, men 3.24; wk 12, women 2.86, men 3.04</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li><math>\leq 1.5</math> dairy svg/d (inclusion criteria)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 4wk, 8wk, and 12wk</li> <li>Weight measured by study personnel</li> </ul>	<p><b>Weight</b>, kg, Mean (SD), kg, Linear regression  <b>Over time:</b> baseline, 4wk, 8wk, 12 wk  <b>Women:</b>            Control: 66.7 (11.4), 67.1 (11.5), 66.9 (11.5), 67.1 (11.4)            Milk: 67.6 (10.0), 68.2 (10.0), 68.2 (10.1), 68.5 (10.1)  <b>Men:</b>            Control: 81.1 (9.1), 81.8 (9.1), 82.2 (9.2), 82.1 (9.5)            Milk: 84.5 (11.8), 85.9 (11.7), 85.6 (11.8), 86.1 (11.8)</p> <p><b>Group*Time Interaction: Milk group gained 0.6 kg more than control group, <math>P&lt;0.005</math></b></p>	<p><b>TEI adjusted:</b> No  <b>Energy Intake</b>, kcal/d, Mean (SD)  <b>Over time:</b> baseline, 12wk  <b>Women:</b>            Control: 1611 (317), 1614 (364)            Milk: 1745 (389), 1834 (376)  <b>Men:</b>            Control: 2114 (432), 2081 (501)            Milk: 2291 (574), 2429 (572)  <b>Group*Time Interaction: Milk group increased energy intake more than control, <math>P=0.037</math></b></p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Randomization method NR</li> <li>No preregistered analysis plan</li> </ul> <p><b>Funding sources:</b>            International Dairy Foods Association</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Chee, 2003<sup>12</sup></b>  <b>RCT, Malaysia</b>  Baseline N=200, Analytic N=173 (Attrition: 14%) Power: NR</p> <p><b>Recruitment:</b> convenience sample</p> <p><b>Participant characteristics: postmenopausal women</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: Mean=6485 kJ/d</li> <li>• Sex (female): 100%</li> <li>• Age: Mean ~59y, range: 55-65y</li> <li>• Race/ethnicity: 100% Chinese</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI, Mean ~23.8; Body fat %, Mean ~35.6%; Lean body mass, Mean~32.8 kg; Weight, Mean~56.6 kg; Height, Mean=1.54 m</li> <li>• Physical activity: "physical activity scores", Mean ~104.8</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Among postmenopausal women, those who consumed high calcium skimmed milk every day for 24 mo did not differ in changes of height, weight, body fat %, or lean body mass compared to a control group.</p>	<p><b>Intervention of interest:</b> High calcium skimmed milk (50g powder reconstituted with 400mL water/d); asked to maintain usual physical activity and dietary patterns; given advice to adjust energy intake to compensate for additional calories provided by milk, n=91</p> <p><b>Comparator:</b> Control: maintain usual diet (&lt;2 glasses/d); asked to maintain usual physical activity and dietary patterns, n=82</p> <p>Other interventions: none</p> <p><u>Intervention duration:</u> 24 mo</p> <p><u>Intervention compliance:</u> Subjects recorded number of milk sachets consumed/d; random home visits and phone calls; Mean=92%, SD=7.9%, Range: 64-100%</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Usual milk intake: &lt;2 glasses/d, 100% (inclusion criteria)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, every 6mo until 24mo follow-up</li> <li>• Height and weight measured by study personnel</li> <li>• Lean body mass measured by DXA</li> <li>• Body fat percentage measured by DXA</li> </ul>	<p><b>Height</b>, linear regression  Control (n=82): "maintained height", Data NR  Milk (n=91): "maintained height", Data NR</p> <p><b>Weight</b>, linear regression  Control (n=82): "maintained weight", Data NR  Milk (n=91): "maintained weight", Data NR</p> <p><b>Body fat %</b>, linear regression  Control (n=82): Changes were not significant, Data NR  Milk (n=91): Changes were not significant, Data NR</p> <p><b>Lean body mass</b>, linear regression  Control (n=82): Changes were not significant, Data NR  Milk (n=91): Changes were not significant, Data NR</p>	<p><b>TEI adjusted:</b> No, but subjects in milk group advised to adjust EI to compensate for additional energy from milk</p> <p><b>Energy intake, kJ/d, Mean (SD)</b>  EI: baseline vs 24mo, within groups:  Control: 6489 (1208) vs 5819 (1312), P&lt;0.05  Milk: 6484 (1259) vs 6169 (1157), P=NS  EI at 24mo, between groups, P=NS</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: SES, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Baseline differences in BMD, may suggest concern with randomization</li> <li>• Differences in attrition and reasons for withdraw between control and intervention groups; no data to see if results are robust despite differences in missing data</li> <li>• No power calculation</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b> New Zealand Milk</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Daly, 2006<sup>13</sup></b>  <b>RCT, Australia</b>  Baseline N=167, Analytic N=149 (Attrition: 10.8%); Power: NR</p> <p><b>Recruitment:</b> community advertisements</p> <p><b>Participant characteristics: older men</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~8808 kJ/d</li> <li>Sex: 100% male</li> <li>Age (y): Mean=61.9, SD=7.7, Range=50-87</li> <li>Race/ethnicity: 100% White</li> <li>SES: NR</li> <li>Anthropometrics: BMI, Mean~26.4 kg/m<sup>2</sup></li> <li>Physical activity: Energy expenditure in moderate activities, Mean~8751 kJ/wk; Weight-bearing activities, Mean~5.5 hr/wk</li> <li>Smoking: Current smokers, 4.8%</li> </ul> <p><b>Summary of findings:</b>  In older men, drinking 400ml of 1%-fat milk over typical intake compared to control group (usual intake) resulted in significantly greater weight at 18mo, however there was no difference in weight between groups at 2 years. There was no change in height over 2 years within or between groups.</p>	<p><b>Intervention:</b> 1% Milk (fortified with calcium and vit D<sub>3</sub>), 400 ml/d in addition to usual milk intake, n=85</p> <p><b>Comparator:</b> Control (usual diet; details NR), n=82</p> <p>Other interventions: none</p> <p><u>Intervention duration:</u> 2-year</p> <p><u>Intervention compliance:</u> percentage of milk tetra packs consumed based on daily diaries, 85.1%</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Fortified milk over and above their typical intake</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 6, 12, 18, and 24mo</li> <li>Weight measured with electronic scale</li> <li>Height measured using stadiometer</li> <li>BMI calculated as kg/m<sup>2</sup></li> </ul>	<p><b>Height</b>, cm, Linear regression  <b>Change over time, within group:</b>  Control: NS, data NR  Milk: NS, data NR  <b>Change over time, between groups:</b>  Control vs. Milk group: NS, data NR</p> <p><b>Weight</b>, kg, Linear regression, Mean (95% CI)  <u>6mo change</u>  <b>Within group:</b>  Control: -0.40, P=NS  Milk: 0.14, P=NS  <b>Between groups:</b> 0.54 (-0.27, 1.36), P=NS</p> <p><u>12mo change</u>  <b>Within group:</b>  Control: 0.01, P=NS  <b>Milk: 0.75, P&lt;0.05</b>  <b>Between groups:</b> 0.74 (-0.17, 1.64), P=NS</p> <p><u>18mo change</u>  <b>Within group:</b>  <b>Control: -1.08 (0.2, 1.9), P&lt;0.001</b>  Milk: 0.18, P=NS  <b>Between groups:</b> 1.26 (0.22, 2.29), P&lt;0.01</p> <p><u>24mo change</u>  <b>Within group:</b>  Control: -0.11, P=NS  Milk: 0.68, P=NS  <b>Between groups:</b> 0.79 (-0.40, 1.97), P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Energy Intake, kJ/d, Mean (SD)</b>  <b>Over time, within group:</b> 0, 12, 24mo  Control: 8603 (2274), 8943 (2285), 8684 (1877), P=NS for all  <b>Milk: 9013 (2342), 9504 (2301), 9208 (1991); baseline &lt; 12 mo, P=0.05</b>  <b>Between groups</b> at baseline, 12, 24 mo: P=NS</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, protein, medications, supplements, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES</li> <li>Other factors considered: timing, temporal use, sugar, fiber, energy density</li> </ul> <p><b>Additional model adjustments:</b>  Bone mineral density, biochemical tests (PTH, serum 25(OH)D, calcium, albumin, creatinine, phosphorus)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Method of allocation concealment NR</li> <li>No power calculation</li> <li>No preregistered data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>  Geoffrey Gardiner Dairy Foundation; Helen M Schutt; Faculty of Health and Behavioural Sciences, Deakin University</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Faghih, 2011<sup>19</sup></b>  <b>RCT, Iran</b>  Baseline N=100, Analytic N=85 (Attrition: 15%); Power: NR</p> <p><b>Recruitment:</b> NR</p> <p><b>Participant characteristics: healthy overweight/obese premenopausal women</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean (SD): Control, 1839.5 kcal/d (169.54); High milk, 1937.26 kcal/d (177.79)</li> <li>Sex (female): 100%</li> <li>Age, Mean (SD): Control, 38.25 y (9.49); High milk, 38.27 y (10.43)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics, Mean (SD): BMI, Control, 30.78 (3.13); High milk, 30.0 (3.55)</li> <li>Physical activity, Mean (SD): Control, 35.48 MET.h/d (4.37); High milk, 33.17 MET.h/d (3.04)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In overweight/obese premenopausal women, drinking 3 svg/d of low-fat milk compared to no milk as part of a controlled diet providing 500 kcal/d deficit for 8wk resulted in greater decreases in weight, BMI, WC, and WHR, but did not change fat mass or body fat %.</p>	<p><b>Intervention of interest:</b> High milk (diet providing 500 kcal/d deficit with 3 svg (220mL)/d of low-fat milk (1.5%)), n=22</p> <p><b>Comparator:</b> Control (diet providing 500 kcal/d deficit), n=20</p> <p>Other interventions: soy milk, calcium supplement</p> <p><u>Intervention duration:</u> 2wk run-in + 8wk intervention; 10wk total study duration</p> <p><u>Intervention compliance:</u> NR</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 8wk follow-up</li> <li>Weight measured using digital scale</li> <li>Height measured using stadiometer</li> <li>WC measured at smallest circumference below rib cage and above the umbilicus</li> <li>Hip circumference measured at largest circumference between waist and knees; WHR: waist-to-hip ratio</li> <li>Fat mass measured using BIA</li> </ul>	<p><b>Weight change (0-8wk)</b>, kg, Mean (SD), Linear regression  <b>Control (n=20): 2.87 (1.55)</b>  <b>High milk (n=22): 4.43 (1.93)</b>  <b>P&lt;0.01</b></p> <p><b>Weight change (0-8wk)</b>, % of initial, Mean (SD), Linear regression  <b>Control (n=20): 3.80 (2.13)</b>  <b>High milk (n=22): 5.80 (2.1)</b>  <b>P&lt;0.01</b></p> <p><b>BMI change (0-8wk)</b>, kg/m<sup>2</sup>, Mean (SD), Linear regression  <b>Control (n=20): 1.15 (0.62)</b>  <b>High milk (n=22): 1.74 (0.73)</b>  <b>P&lt;0.01</b></p> <p><b>WC change (0-8wk)</b>, cm, Mean (SD), Linear regression  <b>Control (n=20): 3.98 (2.77)</b>  <b>High milk (n=22): 6.32 (2.57)</b>  <b>P&lt;0.01</b></p> <p><b>WHR change (0-8wk)</b>, Mean (SD), Linear regression  <b>Control (n=20): 0.021 (0.01)</b>  <b>High milk (n=22): 0.038 (0.01)</b>  <b>P&lt;0.01</b></p> <p><b>Fat mass change (0-8wk)</b>, kg, Mean (SD), Linear regression  Control (n=20): 2.77 (1.29)  High milk (n=22): 3.82 (2.46)  P=NS</p> <p><b>Body fat % change (0-8wk)</b>, Mean (SD), Linear regression  Control (n=20): 2.32 (1.41)  High milk (n=22): 2.92 (2.23)  P=NS</p>	<p><b>TEI adjusted:</b> No (no diff btwn groups)</p> <p><b>Energy intake, kcal/d, Mean (SD)</b>  <b>EI during study, between groups:</b>  <b>Control: 1221.21 (153.73)</b>  <b>High milk: 1297.89 (137.83)</b>  <b>P=0.36</b></p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake, medications, supplements</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Methods for randomization and concealment NR</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  National Nutrition and Food Technology Research Institute; Iran Daru Company provided calcium carbonate capsules</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Fathi, 2016<sup>20</sup></b>  <b>RCT, Iran</b>            Baseline N=75, Analytic N=58 (Attrition: 25%); For 2 groups of interest: Baseline n=50, analytic n= 40 (attrition= 20%); Power: n=18 per group required to detect 3.5 kg difference in 8wk change in weight between groups with 90% and alpha=0.05</p> <p><b>Recruitment:</b> outpatients referred to Cardiovascular Research Center</p> <p><b>Participant characteristics: healthy overweight/obese premenopausal women</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean (95% CI): Control, 2016.7 kcal/d (1970.9, 2062.5); Milk, 2017.7 (1968.4, 2067.0)</li> <li>Sex (female): 100%</li> <li>Age, Mean (95% CI): Control, 36.5 y (34.4, 38.7); Milk, 34.8 y (32.8, 36.8)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics, Mean (95% CI): BMI: Control, 28.9 (28.1, 29.7); Milk, 28.8 (27.9, 29.6)</li> <li>Physical activity: NR; instructed to maintain physical activity level during study</li> <li>Smoking: 100% nonsmokers</li> </ul> <p><b>Summary of findings:</b>            In overweight/obese premenopausal women, drinking 2 svg/d of low-fat milk for 8wk compared to a control group of women who did not drink 2 svg/d resulted in greater decreases in weight, BMI, and WC.</p>	<p><b>Intervention of interest:</b> Milk (diet providing maintenance level of kcal and containing 2 svg/d low-fat dairy and 2 svg/d low-fat milk), n=25</p> <p><b>Comparator:</b> Control (diet providing maintenance level of kcal and containing 2 svg/d low-fat dairy), n=25</p> <p>Other interventions: kefir</p> <p><u>Intervention duration:</u> 2wk run-in followed by 8wk intervention; 10wk total study duration</p> <p><u>Intervention compliance:</u> 100% of study completers consumed ≥90% products, assessed by return of containers at bi-weekly study visits</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 8wk follow-up</li> <li>Weight and height measured by study personnel</li> <li>WC measured at narrowest point between lowest rib and iliac crest (average of 2 measurements)</li> </ul>	<p><b>Intention to treat analyses (control n=25; milk n=25)</b>  <u>Weight</u>, kg, Mean (95% CI), Linear regression            Difference in change, between groups:  <b>Control (ref)</b>  <b>Milk: -0.9 (-1.3, -0.5), P&lt;0.001</b></p> <p><u>BMI</u>, kg/m<sup>2</sup>, Mean (95% CI), Linear regression            Difference in change, between groups:  <b>Control (ref)</b>  <b>Milk: -0.4 (-0.5, -0.2), P&lt;0.001</b></p> <p><u>WC</u>, cm, Mean (95% CI), Linear regression            Difference in change, between groups:  <b>Control (ref)</b>  <b>Milk: -0.9 (-1.5, -0.3), P=0.002</b></p> <p><b>Per protocol analyses (control n=20; milk n=20)</b>  <u>Weight</u>, kg, Mean (95% CI), Linear regression            Difference in change, between groups:  <b>Control (ref)</b>  <b>Milk: -1.2 (-1.6, -0.7), P&lt;0.001</b></p> <p><u>BMI</u>, kg/m<sup>2</sup>, Mean (95% CI), Linear regression            Difference in change, between groups:  <b>Control (ref)</b>  <b>Milk: -0.4 (-0.6, -0.2), P&lt;0.001</b></p> <p><u>WC</u>, cm, Mean (95% CI), Linear regression            Difference in change, between groups:  <b>Control (ref)</b>  <b>Milk: -1.1 (-1.9, -0.3), P=0.003</b></p>	<p><b>TEI adjusted: No</b>  <b>Energy intake, kcal/d, Mean (95% CI)</b>            At 8wk follow-up, between groups:            Control: 2002.5 (1949.4, 2055.6)            Milk: 2004.9 (1945.4, 2064.4)            P=0.921</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, medications, supplements, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density</li> </ul> <p><b>Additional model adjustments:</b>            Dietary calcium at baseline</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Trial registry does not include data analysis plan</li> </ul> <p><b>Funding source:</b>            Shiraz University of Medical Sciences</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Lee, 2016<sup>38</sup></b>  <b>RCT, Korea</b>            Baseline N=66, Analytic N=58 (Attrition: 12%); Power: n=65 at 80% power with a <math>\alpha=0.05</math> to detect differences in systolic blood pressure of 5 mmHg and 20% dropout</p> <p><b>Recruitment:</b> posters, newspaper advertisements, single medical center</p> <p><b>Participant characteristics: adults with metabolic syndrome</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Median~1627 kcal/d</li> <li>Sex (female): 50%</li> <li>Age: Mean~50y, Range=35-65</li> <li>Race/ethnicity: NR</li> <li>SES: Education level: <math>\leq</math>Elementary school: 3%; Middle to high school: 57%; <math>\geq</math>University: 40%; Monthly household income (x 10<sup>4</sup> South Korean Won): &lt;100: 10%; 100-300: 38%; &gt;200: 52%</li> <li>Anthropometrics: Weight, Mean~75.9 kg; BMI, Mean~27.8 kg/m<sup>2</sup>; WC, Mean~95 cm</li> <li>Physical activity: regular exerciser 45%</li> <li>Smoking: Nonsmoker 76%, Current smoker 24%</li> </ul> <p><b>Summary of findings:</b>            In Korean adults with metabolic syndrome, drinking low-fat milk (400 mL/d) compared to habitual diet for 6wk did not result in differences between groups in changes in weight, BMI, WC, HC, or WHR. Energy intake was similar during intervention across groups.</p>	<p><b>Intervention:</b> Low-fat milk (400 mL/d), n=28</p> <p><b>Comparator:</b> No milk: maintain usual dietary pattern, physical activity level, and habitual milk intake (&lt;2 mL/d), n=30</p> <p>Other interventions: none</p> <p><u>Intervention duration:</u> 6wk</p> <p><u>Intervention compliance:</u> examined through self-recorded diaries and phone monitoring; mean compliance ratio in low-fat group was 0.965</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Habitual milk intake &lt;200 mL/d at least 3x/wk (inclusion criteria)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 6wk follow-up</li> <li>Weight and height measured using undisclosed methods</li> <li>BMI calculated as body weight in kg divided by height in meters squared</li> <li>Waist circumference (WC) measured at narrowest point between lowest rib and iliac crest using tape;</li> <li>High WC defined as <math>\geq 90</math> cm for men and <math>\geq 85</math> cm for women</li> <li>Hip circumference (HC) measured using undisclosed methods</li> <li>Waist-to-hip ratio (WHR) calculated using undisclosed method</li> </ul>	<p><b>Weight</b>, kg, Mean (SD), Wilcoxon rank sum  <b>Baseline, Change after 6wk; within group:</b>            No milk: 73.3 (12.1), 0.7 (4.2); P=0.612  <b>Low-fat milk: 78.5 (11.5), 0.5 (1.1); P=0.032</b>  <b>Change over time, between groups:</b>            P=0.225</p> <p><b>BMI</b>, kg/m<sup>2</sup>, Mean (SD), Wilcoxon rank sum  <b>Baseline, Change after 6wk; within group:</b>            No milk: 27.3 (3.2), 0.1 (1.2); P=0.519  <b>Low-fat milk: 28.1 (2.6), 0.2 (0.5); P=0.014</b>  <b>Change, between groups:</b> P=0.252</p> <p><b>WC</b>, cm, Mean (SD), Wilcoxon rank sum  <b>Baseline, Change after 6wk; within group:</b>            No milk: 93 (6.7), -0.4 (2.4); P=0.041            Low-fat milk: 97.1 (6.3), -0.1 (1.5); P=0.829  <b>Change, between groups:</b> P=0.099</p> <p><b>HC</b>, cm, Mean (SD), Wilcoxon rank sum  <b>Baseline, Change after 6wk; within group:</b>            No milk: 100.8 (5.3), -0.1 (1.7); P=0.346            Low-fat milk: 103.5 (4.8), -0.2 (1.2); P=0.469  <b>Change, between groups:</b> P=0.413</p> <p><b>WHR</b>, Mean (SD), Wilcoxon rank sum  <b>Baseline, Change after 6wk; within group:</b>            No milk: 0.9 (0.04), 0.003 (0.02); P=0.261            Low-fat milk: 0.9 (0.04), -0.001 (0.01); P=0.834  <b>Change over time, between groups:</b>            P=0.181</p> <p><b>High WC</b>, N (%), Fisher exact test  <b>At Baseline, At 6wk; within group:</b>            No milk: 27 (90), 26 (86.7); P=1            Low-fat milk: 28 (100), 27 (96.4); P=1  <b>Change, between groups:</b> NS</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Energy Intake</b>, kcal/d  <b>Baseline, median (interquartile range), Change, mean (SD); within group:</b>            No milk: 1607.7 (1051.8, 3343.4), -3.7 (295.1), P=0.833            Low-fat milk: 1645.9 (845.8, 3371.4), 42.5 (420.1), P=0.519  <b>Change over time, between groups:</b>            P=0.388</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, protein, medications, supplements, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity</li> <li>Other factors considered: timing, temporal use, sugar, fiber, energy density</li> </ul> <p><b>Additional model adjustments:</b>            Biomarkers related to inflammation, oxidative stress and atherosclerosis; nutrient intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Baseline differences in weight and WC between groups, suggest issue with randomization</li> <li>6wk study duration</li> <li>Unclear if outcome assessors were aware of intervention assignment</li> <li>Trial registry does not include data analysis plan</li> </ul> <p><b>Funding source:</b>            Ministry of Food and Drug Safety</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Wagner, 2007<sup>57</sup></b>  <b>RCT, United States</b>  Baseline N=80-88, Analytic N=58  (Attrition: 31%); Power: 0.999 for n=12 per group</p> <p><b>Recruitment:</b> NR</p> <p><b>Participant characteristics: ovwt and obese premenopausal adult women</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean ~1415 kcal/d (500 kcal restriction as part of intervention)</li> <li>Sex (female): 100%</li> <li>Age: Mean ~37y</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics, mean: BMI: ~33 kg/m<sup>2</sup> (Range=26-41); Weight: ~198 lbs</li> <li>Physical activity: 3x/wk for 45 min to 1 hr as part of intervention</li> <li>Smoking: 100% non-smokers</li> </ul> <p><b>Summary of findings:</b>  In premenopausal overweight and obese women in a weight loss program that included a 500 kcal total energy intake deficit and supervised physical activity, drinking 20 oz/d 1% milk for 12 weeks resulted in similar reductions in body weight but less fat loss than a placebo group.</p>	<p><b>Intervention:</b> 1% milk (20 oz/d provided; energy intake decreased to account for addition of milk), n=17</p> <p><b>Comparator:</b> Placebo (consumed enough dairy from milk, yogurt, and cheese to produce a dietary intake of 750 mg of daily calcium), n=13</p> <p>Other interventions: calcium lactate supplement, calcium phosphate supplement</p> <p>Intervention methods: 12 wk, double-blind RCT; all subjects advised to consume 500kcal energy deficit and exercise 45-60 mins, 3 times/wk, supervised; compliance monitored by dietitian via daily food records</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk group: 20 oz/d of 1% fat milk provided (participants told they would be given either milk or non-dairy milk-like placebo; milk provided weekly in non-labeled plastic container)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline and weekly for 12wk</li> <li>Body weight</li> <li>Body composition determined using bioelectrical impedance</li> </ul>	<p><b>Body Weight</b>, Paired t-test and ANOVA  <b>Change over time, within group:</b> 0wk, 12wk  <b>Placebo:</b> P&lt;0.01, Data NR  <b>Milk:</b> P&lt;0.01, Data NR  <b>Change over time, between groups:</b>  Placebo vs Milk group: P=NS, Data NR</p> <p><b>Body Fat</b>, Paired t-test and ANOVA  <b>Change over time, within group:</b>  <b>Placebo:</b> P&lt;0.01, Data NR  <b>Milk:</b> P&lt;0.01, Data NR  <b>Change over time, between groups:</b>  <b>Placebo vs Milk group: milk group lost less fat than placebo, Data NR, P&lt;0.05</b></p>	<p><b>TEI adjusted:</b> Yes (controlled via diet)</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, protein, medications, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, fiber, energy density, supplements</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Randomization and allocation concealment not clear</li> </ul> <p><b>Funding source:</b>  Purac of America, Inc.</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<b>MENDELIAN RANDOMIZATION STUDY</b>			
<p><b>Yang, 2017<sup>60</sup></b></p> <p><b>Mendelian Randomization, Genetic Investigation of Anthropometric Traits (GIANT), Country: NR</b></p> <p>Baseline N=NR, Analytic N (BMI data)=324870, Analytic N (WHR data)= 210222 (Attrition: NR%); Power: NR</p> <p><b>Recruitment:</b> NR</p> <p><b>Participant characteristics:</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 54%</li> <li>• Age: NR</li> <li>• Race/ethnicity: European ancestry</li> <li>• SES: NR</li> <li>• Anthropometrics: NR</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b> Genetically predicted milk consumption was positively associated with BMI. Genetically predicted milk consumption was positively associated with waist-to-hip ratio in men but not women.</p>	<p><b>Exposure of interest:</b> Milk intake, genetically predicted based on rs4988235</p> <p><b>Comparator:</b> Milk intake (continuous; 66 g/d)</p> <p>Other exposure measures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• From “dietary questionnaire”; represents milk intake from adolescence</li> <li>• Methods and timing: NR</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Milk intake: NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• Methods and timing: NR</li> <li>• BMI (inverse standard normal transformed)</li> <li>• Waist-hip ratio (inverse standard normal transformed)</li> </ul>	<p><b>BMI:</b> Wald estimate, <math>\beta</math> (95% CI)  <b>Per sd of milk consumption (66 g/d):</b>  <b>All: 0.060 (0.033, 0.087)</b>  <b>Men (n=152,893): 0.068 (0.027, 0.108)</b>  <b>Women (n=171,977): 0.053 (0.013, 0.092)</b></p> <p><b>Waist-to-hip ratio:</b> Wald estimate, <math>\beta</math> (95% CI)  <b>Per sd of milk consumption (66 g/d):</b>  <b>All: 0.030 (-0.0004, 0.061)</b>  <b>Men (n=93,480): 0.049 (0.010, 0.088)</b>  <b>Women (n=116,742): 0.000 (-0.037, 0.037)</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: N/A</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Correction for multiple comparisons</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Bias due to confounding not clear (key confounders not controlled for)</li> <li>• Bias due to selection of participants: No information</li> <li>• Bias due to classification of exposures: No information</li> <li>• Bias due to deviations from intended exposures: No information</li> <li>• Bias due to missing data: No information</li> <li>• Bias due to measurement of outcomes: No information</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  None</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<b>PROSPECTIVE COHORT STUDIES</b>			
<p><b>Babio, 2015<sup>4</sup></b>  <b>Prospective Cohort Study, PREDIMED, Spain</b>  Baseline N=7447, Analytic N=1386 (Attrition: 81%), Power: NR</p> <p><b>Recruitment:</b> via participating PCP medical record; multicenter RCT</p> <p><b>Participant characteristics: older adults with ≥3 CVD risk factors</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~2323 kcal/d</li> <li>Sex (female): 52%</li> <li>Age: Mean ~67y</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI, Mean~28.4; WC (women), Mean~92.4 cm; WC (men), Mean~97.9 cm; Abdominal obesity, 44%</li> <li>Physical activity: Mean~274 METxmin/d</li> <li>Smoking: Former, 26%; Current, 16%</li> </ul> <p><b>Summary of findings:</b>  Total milk, low-fat milk, and whole milk intake was not significantly associated with incidence of abdominal obesity in older adults without metabolic syndrome but ≥ 3 CVD risk factors at baseline.</p>	<p><b>Exposures of interest:</b> Total milk, low-fat milk, whole-fat milk</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Total milk intake (categorical; tertiles)</li> <li>Low-fat milk intake (categorical; tertiles)</li> <li>Whole milk intake (categorical; tertiles)</li> </ul> <p>Other exposures: total dairy, low-fat dairy, whole-fat dairy, cheese</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Semi-quantitative FFQ validated for PREDIMED; Represents habitual intake during follow-up (Median: 3.2y, IQR: 1.9, 5.8)</li> <li>At baseline (2003-09), yearly during follow-up, averaged</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Total milk: Mean~263 g/d; Median=207 g/d</li> <li>Low-fat milk: Mean~230 g/d</li> <li>Whole-fat milk: Mean~39 g/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, yearly during follow-up, follow-up varied 1 – 7y (baseline: 2003-09; end of follow-up: 2010)</li> <li>Waist circumference measured by trained staff</li> <li>Abdominal obesity defined as waist circumference ≥88 cm in women and ≥102 cm in men; measured by trained staff</li> </ul>	<p><b>Total milk intake, categorical <u>Abdominal obesity</u></b>, HR (95% CI), Cox regression  Tertile 1 (ref)  Tertile 2: 1.02 (0.83, 1.26)  Tertile 3: 1.08 (0.86, 1.36)  P-trend=0.49</p> <p><b>Low-fat milk intake, categorical <u>Abdominal obesity</u></b>, HR (95% CI), Cox regression  Tertile 1 (ref)  Tertile 2: 1.11 (0.89, 1.33)  Tertile 3: 0.96 (0.78, 1.18)  P-trend=0.66</p> <p><b>Whole-fat milk intake, categorical <u>Abdominal obesity</u></b>, HR (95% CI), Cox regression  Tertile 1 (ref)  Tertile 2: 0.87 (0.71, 1.08)  Tertile 3: 0.97 (0.78, 1.19)  P-trend=0.91</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, medications, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Consumption of vegetables, fruit, legumes, cereals, fish, red meat, biscuits, olive oil, and nuts during follow-up, intervention group</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Start of follow-up and exposure do not coincide</li> <li>Whether missing data was related to exposure group was not reported</li> <li>No a priori analysis plan for this secondary analysis</li> <li>Levels of milk intake in tertiles were not described</li> </ul> <p><b>Funding sources:</b>  Spanish Ministry of Health; Thematic Network; European Regional Development Fund; Catalan Nutrition Center of the Institute of Catalan Studies</p>



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<p><b>Bes-Rastrollo, 2008<sup>9</sup></b>  <b>Prospective Cohort Study, Nurses' Health Study II, United States</b>  Baseline N=116,671, Analytic N=50,026 (Attrition: 57%); Power: NR</p> <p><b>Recruitment:</b> convenience sample of nurses from 14 states</p> <p><b>Participant characteristics: Women</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d, Mean (SE): 1771 (522)</li> <li>Sex (female): 100%</li> <li>Age, y, Mean (SD): 36.5 (4.6)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics, Mean (SD): BMI=24.2 (5.0); Weight, kg=65.9 (14.3)</li> <li>Physical activity, MET-h/wk, Mean (SD): 20.4 (26.4)</li> <li>Smoking: Current, 11.1%</li> </ul> <p><b>Summary of findings:</b>  Among women, 8-year change in milk intake was not significantly associated with 8-year weight change.</p>	<p><b>Exposure of interest:</b> Skim milk, Milk</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Skim milk intake (categorical; tertiles) <ul style="list-style-type: none"> <li>Lowest tertile 8y change (ref)</li> <li>Highest tertile 8y change</li> </ul> </li> <li>Milk intake (categorical; tertiles) <ul style="list-style-type: none"> <li>Lowest tertile 8y change (ref)</li> <li>Highest tertile 8y change</li> </ul> </li> </ul> <p>Other exposures: low calorie cola, low calorie caffeine free cola, water, tea, decaffeinated coffee, coffee, tomato juice, caffeine free cola, cola, orange juice, apple juice, other carbonated beverages, punch</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Self-administered semi-quantitative FFQ; Represents intake during previous year</li> <li>At baseline, 8y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 8y follow-up</li> <li>Weight, self-reported through biennial questionnaires</li> </ul>	<p><b>Skim milk intake, categorical Weight</b>, Linear regression  8y change in weight by 8y change in intake, between group:  Lowest tertile (ref) vs Highest tertile: Data NR, P=NS</p> <p><b>Milk intake, categorical Weight</b>, Linear regression  8y change in weight by 8y change in intake, between group:  Lowest tertile (ref) vs Highest tertile: Data NR, P=NS</p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Postmenopausal hormone use, oral contraceptive use, changes in confounders between time periods</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposures were not well described</li> <li>Impact of missing data on analyses unclear</li> <li>Self-reported weight</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH; Spanish Ministry of Education; Fundacion Caja Madrid; Amigos de la Universidad de Navarra; AHA Established Investigator Award</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Beydoun, 2018<sup>10</sup></b>  <b>Prospective Cohort Study, Healthy Aging in Neighborhoods of Diversity across the Life Span, United States</b>  Baseline N=3720, Analytic N=1371 (Attrition: 63%) Power: NR</p> <p><b>Recruitment:</b> probability sample of 13 neighborhoods</p> <p><b>Participant characteristics:</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d, Mean (SE): 2003 (26)</li> <li>Sex (female): 59.4%</li> <li>Age, y, Mean (SE): 48.4 (0.24)</li> <li>Race/ethnicity: African-American, 58.6%</li> <li>SES: Above poverty, 60.1%; Education: &lt;HS: 6.8%, HS: 56.6%, &gt;HS: 36.6%</li> <li>Anthropometrics: BMI ≥30, 42.1%; Central obesity, 59.8%</li> <li>Physical activity: NR</li> <li>Smoking: Current, 40.5% (missing 8.1%)</li> </ul> <p><b>Summary of findings:</b>  Higher milk intake in men, but not women, was associated with a lower 5 year HR for incident central obesity, whereas higher milk intake in whites was associated with a higher 5 year HR for incident central obesity. All other associations for central obesity and all associations for obesity were non-significant.</p>	<p><b>Exposure of interest:</b> Total milk intake (whole and reduced fat)</p> <p><b>Comparator:</b> Total milk intake (continuous; svg/d)</p> <ul style="list-style-type: none"> <li>Baseline</li> <li>Annual rates of change</li> </ul> <p>Other exposures: yogurt, cheese, total dairy</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Two, 24-hr recalls using the USDA Automated Multiple Pass Method administered by trained interviewers; Represents usual intake</li> <li>At baseline, 5y follow-up; Follow-up time, y, Mean (SE): 4.62 (0.95)</li> </ul> <p><b>Study beverage intake, Mean (SE):</b></p> <ul style="list-style-type: none"> <li>Total milk (svg/d): 0.51 (0.02)</li> <li>Total milk (g/d): 64.3 (2.9)</li> <li>Whole milk (g/d): 32.4 (2.2)</li> <li>Low fat/fat free milk (g/d): 31.8 (2.2)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At 5y follow-up:</li> <li>Height and weight measured by study personnel to calculate BMI</li> <li>Waist circumference (WC) measured using measuring tape, starting from hip bone and wrapping around waist to navel-level)</li> <li>Obesity defined as BMI ≥30</li> <li>Central obesity defined as waist circumference ≥40in in men and ≥35in in women</li> </ul>	<p><b>Total milk intake, continuous Incident obesity</b>, among non-obese at baseline, HR (95% CI), Cox proportional hazards regression  Per svg/d increase in baseline or annual change in milk intake:  <b>All subjects</b> (N=859)  Baseline: 0.98 (0.90, 1.06)  Change: 0.76 (0.51, 1.15)  <b>Men</b>  Baseline: 0.94 (0.81, 1.10)  Change: 0.61 (0.31, 1.21)  <b>Women</b>  Baseline: 1.05 (0.91, 1.22)  Change: 1.00 (0.53, 1.88)  <b>White</b>  Baseline: 0.92 (0.79, 1.06)  Change: 0.59 (0.32, 1.08)  <b>African-American</b>  Baseline: 1.14 (0.98, 1.34)  Change: 1.24 (0.64, 2.45)</p> <p><b>Incident central obesity</b>, among those who were did not have central obesity at baseline, HR (95% CI), Cox proportional hazards regression  Per svg/d increase in baseline or annual change in milk intake  <b>All subjects</b> (N=588)  Baseline: 1.00 (0.75, 1.36)  Change: 1.01 (0.75, 1.36)  <b>Men</b>  <b>Baseline: 0.89 (0.79, 0.99)</b>  Change: 0.82 (0.50, 1.32)  <b>Women</b>  Baseline: 1.07 (0.94, 1.21)  Change: 0.97 (0.60, 1.57)  <b>White</b>  <b>Baseline: 1.14 (1.00, 1.29)</b>  Change: 1.10 (0.69, 1.76)  <b>African-American</b>  Baseline: 0.87 (0.75, 1.00)  Change: 0.76 (0.44, 1.34)</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, smoking</li> <li>Other factors considered: total energy intake, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: anthropometry at baseline, physical activity</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Alcohol, current drug use, self-rated health, total fruit, dark green vegetables, deep yellow vegetables, whole grains, non-whole grains, legumes, nuts/seeds, soy, total meat/poultry/fish, eggs, discretionary solid fat, discretionary oils, added sugars, caffeine</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Baseline and time to follow-up varied</li> <li>Only ~1/3 of original participants with complete data</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  Intramural Research Program NIH/NIA</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b><u>Drapeau, 2004</u></b><sup>16</sup></p> <p><b>Prospective Cohort Study, Quebec Family Study, Canada</b></p> <p>Baseline N=NR, Analytic N=248 (Attrition: NR); Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 54.9%</li> <li>• Age: Mean=39.6 y, SEM=0.9, Range: 18-65</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI, Mean=25.3, SEM=0.3, Range: 17.4-55.6</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>Change in low-fat and regular milk intake not associated with change in weight and adiposity measures over 6 years in adults.</p>	<p><b>Exposure of interest:</b> Low-fat milk (skimmed and partly skimmed milk), Regular milk (whole milk)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>• Low-fat milk intake (continuous; units NR)</li> <li>• Regular milk intake (continuous; units NR)</li> </ul> <p>Other exposures: fruit beverage, fruit juice, regular sodas</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Three-day dietary record (2 weekdays, 1 weekend day); Represents usual intake</li> <li>• At baseline, 6y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• Weight measured by study personnel</li> <li>• Body fat percentage estimated using underwater weighing technique and the Siri formula</li> <li>• Waist circumference measured by study personnel using Airlie Conference procedures</li> <li>• Sum of 6 skinfold thicknesses (triceps, biceps, medial calf, subscapular, suprailiac, and abdominal) measured by study personnel</li> </ul>	<p><b>Low-fat milk intake, continuous</b></p> <p>6y change by 6y change in intake, linear regression</p> <p><u>Weight:</u> NS, Data NR</p> <p><u>Body fat percentage:</u> NS, Data NR</p> <p><u>Waist circumference:</u> NS, Data NR</p> <p><u>Sum of 6 skinfold thicknesses:</u> NS, Data NR</p> <p><b>Regular milk intake, continuous</b></p> <p>6y change by 6y change in intake, linear regression</p> <p><u>Weight:</u> NS, Data NR</p> <p><u>Body fat percentage:</u> NS, Data NR</p> <p><u>Waist circumference:</u> NS, Data NR</p> <p><u>Sum of 6 skinfold thicknesses:</u> NS, Data NR</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, anthropometry at baseline, physical activity</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, race/ethnicity, SES, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Did not account for all key confounders</li> <li>• Validation of 3-day dietary record unclear</li> <li>• No information on missing data</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b></p> <p>Canadian Institutes of Health Research</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Duffey, 2010<sup>18</sup></b>  <b>Prospective Cohort Study, Coronary Artery Risk Development in Young Adults (CARDIA), United States</b>  Baseline N=5115, Analytic N=2444 (Attrition: 52%); Power: NR</p> <p><b>Recruitment:</b> convenience sample through phone and door-to-door recruitment</p> <p><b>Participant characteristics: young adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR; energy from food, Mean: 2347 kcal</li> <li>Sex (female): 53.5%</li> <li>Age, Mean (SD): 25.0 y (3.6)</li> <li>Race/ethnicity: Black 47.4%</li> <li>SES: NR</li> <li>Anthropometrics, Mean (SD): BMI, 24.5 (5.0); WC, 77.3 cm (10.9)</li> <li>Physical activity, Mean (SD): 429 exercise units/wk (302)</li> <li>Smoking: Current 28.1%, Former 13.1%, Never 58.7%</li> </ul> <p><b>Summary of findings:</b>  Low-fat and whole-fat milk intake was not associated with incidence of high WC at 20y follow-up.</p>	<p><b>Exposure of interest:</b> Low-fat milk (skim and <math>\leq 2\%</math> fat), Whole-fat milk (<math>\geq 3\%</math> fat)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Low-fat milk intake (continuous; kcal/d)</li> <li>Low-fat milk intake (categorical; quartiles)</li> <li>Whole-fat milk intake (continuous; kcal/d)</li> <li>Whole-fat milk intake (categorical; quartiles)</li> </ul> <p>Other exposures: fruit juice, SSBs</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Semi-quantitative, interviewer-administered, validated diet history food-frequency questionnaire; Represents previous month</li> <li>At baseline, 7y follow-up (averaged)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Low-fat milk: 61% consuming <ul style="list-style-type: none"> <li>Among consumers: Mean=160 kcal/d, SE=4</li> </ul> </li> <li>Whole-fat milk: 47% consuming <ul style="list-style-type: none"> <li>Among consumers: Mean=204 kcal/d, SE=6</li> </ul> </li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At 20y follow-up</li> <li>WC at minimum abdominal girth measured in duplicate; High WC defined as WC&gt;88cm (women) or &gt;102cm (men)</li> </ul>	<p><b>Milk intake, categorical</b>  <b>High WC</b>, Poisson regression, RR (95% CI)  <b>Low-fat milk:</b> 1.02 (0.95, 1.08), P for trend = 0.639  <b>Whole-fat milk:</b> 1.06 (0.98, 1.13), P for trend = 0.143</p> <p><b>Milk intake, continuous</b>  <b>High WC</b>, Poisson regression, RR (95% CI)  <b>Low-fat milk:</b> 1.02 (0.97, 1.07)  <b>Whole-fat milk intake:</b> 1.02 (0.98, 1.07)</p>	<p><b>TEI adjusted:</b> Yes (energy from food and other beverages)</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake (energy from food and other beverages), alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  CARDIA exam center</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Did not account for all key confounders</li> <li>Validity of 3-day diet record unclear</li> <li>Impact of missing data on analyses unclear</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Danone Research Center; NIH; UNC-CH Center for Environmental Health and Susceptibility; UNC-CH Clinic Nutrition Research Center; Carolina Population Center</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Fresan, 2016<sup>22</sup></b>  <b>Prospective Cohort Study, SUN Cohort, Spain</b>  Baseline N=17984 Analytic N=15,765 (Attrition: 12%); Power: NR</p> <p><b>Recruitment:</b> Convenience sample of university graduates</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean (SD): ~2342 kcal/d</li> <li>Sex (female): 59.8%</li> <li>Age, Mean (SD): 37.9y (11.7)</li> <li>Race/ethnicity: NR</li> <li>SES: University graduate 100%</li> <li>Anthropometrics, Mean (SD): BMI, 23.49 (3.5)</li> <li>Physical activity, Mean (SD): ~21.7 MET-h/wk</li> <li>Smoking: Current smoker 21.6%, Former smoker 28.4%</li> </ul> <p><b>Summary of findings:</b>  Replacement of skim, reduced-fat, or whole milk, or milk shakes with water was not significantly associated with incidence of obesity or 4y weight change.</p>	<p><b>Exposure of interest:</b> Skim milk, Whole milk, Reduced fat milk, Milk shake (1svg = 200mL)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Substituting water for skim milk (continuous; svg/d)</li> <li>Substituting water for whole milk (continuous; svg/d)</li> <li>Substituting water for reduced-fat milk (continuous; svg/d)</li> <li>Substituting water for milk shake (continuous; svg/d)</li> </ul> <p>Other exposures: SSBs, bottled juice, diet soda beverages, regular coffee, decaffeinated coffee, fresh non-orange fruit juice, fresh orange juice, water</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Semi-quantitative FFQ previously validated in Spain; Represents intake during previous year</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Dairy products: Mean~9.6 svg/wk</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, every 2y</li> <li>BMI from self-reported weight and height</li> <li>Obesity defined as BMI ≥30 kg/m<sup>2</sup></li> </ul>	<p><b>Substitution of 1 svg/d water for 1 svg/d skim milk, continuous</b>  <b>Obesity</b>, OR (95% CI), logistic regression 0.94 (0.87, 1.03)  <b>4y Weight change</b>, g, Mean (95% CI), linear regression 28 (-82, 137)</p> <p><b>Substitution of 1 svg/d water for 1 svg/d reduced-fat milk, continuous</b>  <b>Obesity</b>, OR (95% CI), logistic regression 1.06 (0.96, 1.16)  <b>4y Weight change</b>, g, Mean (95% CI), linear regression 6 (-100, 113)</p> <p><b>Substitution of 1 svg/d water for 1 svg/d whole milk</b>  <b>Obesity</b>, OR (95% CI), logistic regression 0.96 (0.87, 1.06)  <b>4y Weight change</b>, g, Mean (95% CI), linear regression 61 (-55, 177)</p> <p><b>Substitution of 1 svg/d water for 1 svg/d milk shake, continuous</b>  <b>Obesity</b>, OR (95% CI), logistic regression 1.32 (0.79, 2.22)  <b>4y Weight change</b>, g, Mean (95% CI), linear regression -399 (-1049, 250)</p>	<p><b>TEI adjusted:</b> Adjusted for EI from sources other than exchanged beverages</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity,</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Personal history of obesity, family history of obesity, following a special diet, adherence to Mediterranean dietary pattern, snacking between meals, weight change in past 5y</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Selection into study may have been related to exposure and outcome</li> <li>Weight self-reported</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Spanish Ministry of Health; Navarra Regional Government; University of Navarra</p>

**Funtikova, 2015<sup>23</sup>**

**Prospective Cohort Study, Spain**

Baseline N=3,058, Analytic N=2,112  
(Attrition: 31%); Power: NR

**Recruitment:** Randomly selected  
population-based sample

**Participant characteristics: adults**

- Total energy intake, Mean: ~11.2 MJ/d kcal/d
- Sex (female): 52.6%
- Age, Mean: ~49.2y
- Race/ethnicity: NR
- SES: Higher education ~37%
- Anthropometrics, Mean: WC, ~89.6 cm
- Physical activity, Mean: ~200 MET-min/d (leisure time)
- Smoking: Current smoker ~26%

**Summary of findings:**

In adults, whole milk consumption of <1 serving/d was associated with greater odds of abdominal obesity 10 years later compared to not drinking whole milk; however, there was no significant association between whole milk consumption of ≥1 servings/d on abdominal obesity 10 years later compared to not drinking whole milk. Skim and low-fat milk intake were not associated with WC or incidence of abdominal obesity.

**Exposure of interest:** Whole milk (4% fat), Skim and Low-fat milk (1 svg = 200mL)

**Comparators:**

- Whole milk intake (continuous; 100 kcal/d)
- Whole milk intake (categorical; svg/d)
  - No consumption (ref), <1, ≥1
- Whole milk intake change (categorical)
  - No consumption (ref), Decrease, Increase, Maintain
- Skim and low-fat milk intake (continuous; 100 kcal/d)
- Skim and low-fat milk intake (categorical; svg/d)
  - No consumption (ref), <1, ≥1
- Skim and low-fat milk intake change (categorical)
  - No consumption (ref), Decrease, Increase, Maintain

Other exposures: soft drinks, juices

**Exposure assessment method and timing:**

- Validated, 166-item FFQ administered by trained interviewer; Represents intake during previous year
- At baseline, 9y follow-up

**Study beverage intake:**

- Whole milk, mL/d, mean (SD): 63 (131); no consumption: 66%, <1 svg/d: 13%, ≥1 svg/d: 21%
- Skim and low-fat milk, mL/d, mean (SD): 115 (178); no consumption: 54%, <1 svg/d: 12%, ≥1 svg/d: 34%

**Whole milk, continuous**

**WC**, cm, Change per 100 kcal/d increase, Mean (95% CI), linear regression:  
-0.19 (-0.66, 0.28), P=0.42  
**Men:** -0.38 (-1.02, 0.26), P=0.25  
**Women:** 0.06 (-0.63, 0.74), P=0.87

**Whole milk change, categorical**

**WC**, cm, Change in WC by change in consumption, Mean (95% CI), linear regression:  
No consumption (ref)  
Decrease: -0.03 (-1.00, 0.94), P=0.95  
Increase: -0.26 (-1.56, 1.04), P=0.69  
Maintain: -0.68 (-2.05, 0.70), P=0.33  
**Men (n=1000)**  
No consumption (ref)  
Decrease: -1.13 (-2.39, 0.13), P=0.08  
**Increase: -1.69 (-3.27, -0.12), P=0.036**  
Maintain: -1.56 (-3.22, 0.09), P=0.06  
**Women (n=1112)**  
No consumption (ref)  
Decrease: 1.05 (-0.41, 2.51), P=0.16  
Increase: 1.46 (-0.64, 3.57), P=0.17  
Maintain: 0.35 (-1.92, 2.61), P=0.77

**Whole milk, categorical**

**Abdominal obesity**, OR (95% CI), logistic regression  
Incidence by baseline intake:  
No consumption (ref)  
**<1 svg/d: 1.58 (1.07, 2.32)**  
≥1 svg/d: 1.00 (0.72, 1.40)  
**Men (n=756)**  
No consumption (ref)  
<1 svg/d: 1.32 (0.74, 2.38)  
≥1 svg/d: 1.25 (0.75, 2.08)  
P for trend=0.34  
**Women (n=723)**  
No consumption (ref)  
**<1 svg/d: 1.90 (1.13, 3.20)**  
≥1 svg/d: 1.21 (0.78, 1.88)  
P for trend=0.20

**TEI adjusted:** Yes

**Confounders accounted for:**

- Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking
- Other factors considered: total energy intake

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:**

Modified Mediterranean diet score, energy under-and over-reporting, dieting (change in consumption models only), other beverage intake

**Limitations:**

- Not all key confounders accounted for
- Attrition 31% without information on non-completers
- No preregistered analysis plan

**Funding sources:**

Catalan Government; Carlos III Health Institute European Fund for Regional Development; Catalanian Agency for the Administration of University and Research Grants

**Outcome assessment  
methods/timing:**

- At baseline, 9y follow-up
- WC measured midway between lowest rib and iliac crest with participant lying horizontally
- Abdominal obesity defined as >102 cm for men and >88 cm for women

**Skim and low-fat milk, continuous**

**WC**, cm, Mean (95% CI), linear regression

Change per 100 kcal/d increase:

0.25 (-0.30, 0.79), P=0.37

**Men:** 0.27 (-0.55, 1.08), P=0.52

**Women:** 0.30 (-0.45, 1.04), P=0.44

**Skim and low-fat milk change, categorical**

**WC**, cm, Change by change in consumption, Mean (95% CI), linear regression:

No consumption (ref)

Decrease: 0.39 (-0.68, 1.47), P=0.47

Increase: 0.40 (-0.64, 1.43), P=0.45

Maintain: 0.31 (-0.73, 1.35), P=0.56

***Men (n=1000)***

No consumption (ref)

Decrease: 0.49 (-0.92, 1.90), P=0.52

Increase: 0.12 (-1.18, 1.42), P=0.42

Maintain: 0.33 (-1.18, 1.83), P=0.58

***Women (n=1112)***

No consumption (ref)

Decrease: 0.40 (-1.21, 2.01), P=0.47

Increase: 0.74 (-0.89, 2.37), P=0.45

Maintain: 0.42 (-1.07, 1.91), P=0.56

**Skim and low-fat milk, categorical**

**Abdominal obesity**, OR (95% CI), logistic regression

Incidence by baseline intake:

No consumption (ref)

<1 svg/d: 0.76 (0.49, 1.18)

≥1 svg/d: 0.94 (0.69, 1.27)

***Men (n=756)***

No consumption (ref)

<1 svg/d: 0.67 (0.35, 1.31)

≥1 svg/d: 0.77 (0.46, 1.28)

P for trend=0.18

***Women (n=723)***

No consumption (ref)

<1 svg/d: 0.85 (0.47, 1.54)

≥1 svg/d: 0.95 (0.66, 1.35)

P for trend=0.69

#### Guerendiain, 2019<sup>24</sup>

#### **Prospective Cohort Study, Ecuador ("healthy program" intervention with exercise classes and nutrition advice)**

Baseline N=60, Analytic N=31 (Attrition:  
48%); Power: NR

**Recruitment:** convenience sample of  
university employees

#### **Participant characteristics: adults participating in an exercise RCT**

- Total energy intake: NR
- Sex (female): 81.2%
- Age, Mean (SD): 38.97 y (7.45)
- Race/ethnicity: NR
- SES: Occupation, Academics  
40.58%, Administrative 59.42 %
- Anthropometrics: BMI, Mean~26.3
- Physical activity: <150 min/wk  
moderate-vigorous exercise  
(inclusion criteria); randomized to  
Zumba or Zumba and resistance  
exercise
- Smoking: NR

#### **Summary of findings:**

In adults participating in an exercise RCT,  
milk intake at baseline was not associated  
with 16wk changes in weight, BMI, sum of  
6 skinfolds, fat mass, muscle mass, or  
waist-hip index.

#### **Exposure of interest: Milk**

#### **Comparators:**

- Milk intake (categorical; tertiles)
  - T1 ( $\leq 133.33$  g/d)
  - T2 (133.34-250.00 g/d)
  - T3 ( $> 250.00$  g/d)
- Milk intake (continuous; mL/d)
  - Per tertiles of BMI change

Other exposures: cheese, total dairy

#### Exposure assessment method and timing:

- Three-day dietary record (2  
weekdays, 1 weekend day), self-  
administered; Represents usual  
intake
- At baseline

#### **Study beverage intake:**

- Milk intake (g/d), tertiles: T1:  
 $\leq 133.33$ , T2: 133.34-250.00, T3:  
 $> 250.00$

#### **Outcome assessment methods/timing:**

- At baseline, 16wk follow-up
- Height and weight measured by  
study personnel
- Sum of 6 skinfold thickness  
measured using ISAK procedures
- Waist and hip perimeters measured  
by study personnel
- Waist-hip index calculated from  
coefficient between waist and hip  
perimeters using protocol from WHO
- Percentage body fat mass estimated  
using the Faulkner equation
- Muscle mass estimated using  
methodology of four compartments  
(De Rose and Guimaraes, 1980)

#### **Milk intake, categorical**

**Weight** (kg), change from 0-16wk by tertile  
of milk intake at baseline; Mean (SD), linear  
regression

T1 (n=8): -0.65 (1.68)  
T2 (n=12): -0.21 (1.45)  
T3 (n=11): -0.25 (2.95)  
P=0.918, d: -0.18 (95% CI: -1.33, 0.96)

**BMI** (kg/m<sup>2</sup>), change from 0-16wk by tertile  
of milk intake at baseline; Mean (SD), linear  
regression

T1 (n=8): -0.23 (0.64)  
T2 (n=12): -0.09 (0.88)  
T3 (n=11): 0.25 (1.49)  
P=0.585, d: -0.37 (95% CI: -1.28, 0.54)

**Sum of 6 skinfolds** (mm), change from 0-  
16wk by tertile of milk intake at baseline;  
Mean (SD), linear regression: T1 (n=8): -  
36.04 (6.46)  
T2 (n=12): -25.23 (18.44)  
T3 (n=11): -38.69 (11.66)  
P=0.108, d: 0.17 (95% CI: -0.44, 0.78)

**Fat mass** (kg), change from 0-16wk by  
tertile of milk intake at baseline; Mean (SD),  
linear regression:

T1 (n=8): -2.78 (0.89)  
T2 (n=12): -1.91 (1.62)  
T3 (n=11): -2.98 (1.83)  
P=0.250, d: 0.13 (95% CI: -0.84, 1.10)

**Fat mass** (%), change from 0-16wk by  
tertile of milk intake at baseline; Mean (SD),  
linear regression: T1 (n=8): -4.06 (1.12)

T2 (n=12): -2.91 (2.28)  
T3 (n=11): -3.97 (1.41)  
P=0.214, d: -0.05 (95% CI: -0.77, 0.67)

**Muscle mass** (kg), change from 0-16wk by  
tertile of milk intake at baseline; Mean (SD),  
linear regression:

T1 (n=8): 2.36 (1.29)  
T2 (n=12): 1.85 (1.25)  
T3 (n=11): 2.97 (1.92)  
P=0.105, d: -0.37 (95% CI: -1.38, 0.63)

**TEI adjusted:** No

#### **Confounders accounted for:**

- Key confounders: physical activity  
(type of exercise intervention)
- Other factors considered: none

#### **Confounders NOT accounted for:**

- Key confounders: sex, age,  
race/ethnicity, SES, anthropometry  
at baseline, physical activity,  
smoking
- Other factors considered: total  
energy intake, timing, temporal  
use, sugar, protein, fiber, energy  
density, medications, supplements,  
alcohol

**Additional model adjustments:** N/A

#### **Limitations:**

- Not all key confounders accounted  
for
- Three day dietary record used to  
assess milk intake
- Participants underwent nutrition  
education and physical activity "co-  
exposure"
- Attrition 48% without information on  
non-completers
- No preregistered data analysis plan

#### **Funding sources:**

National University of Chimborazo;  
University of Granada Plan Propio de  
Investigacion 2016



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
		<p><b>Muscle mass</b> (%), change from 0-16wk by tertile of milk intake at baseline; Mean (SD), linear regression:  T1 (n=8): 4.10 (3.05)  T2 (n=12): 3.05 (2.17)  T3 (n=11): 4.15 (1.40)  P=0.211, d: -0.03 (95% CI: -0.76, 0.70)</p> <p><b>Waist-hip index</b>, change from 0-16wk by tertile of milk intake at baseline; Mean (SD), linear regression:  T1 (n=8): -0.00 (0.05)  T2 (n=12): 0.00 (0.03)  T3 (n=11): 0.00 (0.02)  P=0.847, d: -0.13 (95% CI: -1.03, 0.77)</p>	

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Guo, 2018<sup>25</sup></b>  <b>Prospective Cohort Study, Caerphilly</b>  <b>Prospective Cohort Study, UK</b>  Baseline N=2398, Analytic N=1690  (Attrition: 30%); Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: adult men</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean: ~9.6 MJ/d</li> <li>Sex (female): 0%</li> <li>Age, Mean: ~52y</li> <li>Race/ethnicity: NR</li> <li>SES: Manual workers, ~64%</li> <li>Anthropometrics: BMI, Mean~26.3</li> <li>Physical activity: Leisure activity, ~48%</li> <li>Smoking: Current ~52%</li> </ul> <p><b>Summary of findings:</b>  In men, milk intake was not associated with 5y and 10y changes in BMI.</p>	<p><b>Exposure of interest:</b> Milk</p> <p><b>Comparators:</b> Milk intake (categorical; quartiles)</p> <ul style="list-style-type: none"> <li>Q1 (0 g/d)</li> <li>Q2 (0 - 293 g/d)</li> <li>Q3 (294 - 585 g/d)</li> <li>Q4 (&gt; 585 g/d)</li> </ul> <p>Other exposures: total dairy, cheese, cream, butter</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>50 item semi-quantitative FFQ validated against 7d weighed dietary record by subset of participants at baseline; Represents usual intake</li> <li>At baseline, 5y follow-up, 10y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk, Mean: ~297.9 g/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 5y follow-up, 10y follow-up</li> <li>Weight and height measured by study personnel</li> </ul>	<p><b>Milk intake, categorical BMI</b>, kg/m<sup>2</sup>, Change based on milk intake quartiles at baseline; Mean (SE), linear regression</p> <p><b>At 5y:</b>  Q1 (n=92; ref)  Q2 (n=773): 0.135 (0.164)  Q3 (n=687): 0.041 (0.166)  Q4 (n=110): 0.106 (0.213)  P for trend, 0.664</p> <p><b>At 10y:</b>  Q1 (n=68; ref)  Q2 (n=648): 0.133 (0.240)  Q3 (n=595): -0.053 (0.243)  Q4 (n=93): 0.203 (0.307)  P for trend, 0.523</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Sugar intake, red meat intake, egg intake, incident diabetes, cancer, hypertension, cardiovascular disease</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Start of follow-up and exposure do not coincide (Phase 1 n=1951; Phase 2 (5y later) n=447)</li> <li>Attrition 30% and information on non-completers not reported</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  No external funding</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Holmberg, 2013<sup>28</sup></b>  <b>Prospective Cohort Study, Sweden</b>  Baseline N=2350, Analytic N=1238  (Attrition: 47%); Power: NR</p> <p><b>Recruitment:</b> all male farmers from 9 rural municipalities and non-farmer rural referents, from National Population Register</p> <p><b>Participant characteristics: men living in rural Sweden</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 0%</li> <li>• Age, Mean (SD): 50.3 (6.0) y</li> <li>• Race/ethnicity: NR</li> <li>• SES: Education level, 41.6% Mandatory school, 31.7% Vocational school, 10.7% Secondary school, 7.1% College, 9.0% University</li> <li>• Anthropometrics: BMI: 26.4 (3.2); Normal weight: 35.6%, Overweight: 50.3%, Obese: 14.1%; WHR ≥1: 6.5%</li> <li>• Physical activity: 28.8% sedentary, 56.4% low, 14.8% moderate or vigorous</li> <li>• Smoking: 23.3% daily smokers</li> </ul> <p><b>Summary of findings:</b>  Among men living in rural Sweden, consumption of high fat milk was associated with lower odds of incident central obesity 12 years later compared to low fat milk in unadjusted analyses.</p>	<p><b>Exposure of interest:</b> Type of milk (non-homogenized farm milk, full fat milk with 3% fat, semi-skimmed with 1.5% fat, skimmed with 0.5% fat)</p> <p><b>Comparators:</b> Type of milk (categorical; fat content)</p> <ul style="list-style-type: none"> <li>• Low fat milk (1.5% fat or less), n=609</li> <li>• High fat milk (full fat milk), n=629</li> </ul> <p>Other exposures: spreads, whipping cream, low fat dairy, medium fat dairy, high fat dairy</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• 15 item questionnaire on food choices; represents typical intake</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Milk type: 48.9% low fat, 51.1% high fat</li> </ul> <p><b>Outcomes assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 12y follow-up</li> <li>• Waist circumference measured at level of umbilicus</li> <li>• Hip circumference measured at widest part of the hips</li> <li>• Central obesity defined as WHR ≥1</li> </ul>	<p><i>Milk type, categorical</i>  <b>Incident central obesity</b>, OR (95% CI), logistic regression  By milk fat consumed, between groups:  Low fat (ref)  <b>High fat: 0.64 (0.47, 0.88)</b></p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Dietary assessment not validated</li> <li>• Attrition 47% with no information on those lost to follow-up</li> <li>• No pre-registered data analysis plan</li> </ul> <p><b>Funding sources:</b>  AFA Insurance; LRF Research Foundation; Swedish Council for Working Life and Social Research; Kronoberg County Council</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Johansson, 2018<sup>30</sup></b>  <b>Prospective Cohort Study, Vasterbotten Intervention Programme, Sweden</b>  Baseline N=90,512, Analytic N=27,682 (Attrition: 69%); Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 51.3%</li> <li>Age: 8% 29-34y, 45% 35-44y, 28% 45-54y, 18% 55-65y</li> <li>Race/ethnicity: NR</li> <li>SES: 31% academic education (highest level)</li> <li>Anthropometrics, Mean: BMI ~25.7</li> <li>Physical activity: 17.4% inactive at leisure time</li> <li>Smoking: 20% present smoker</li> </ul> <p><b>Summary of findings:</b>  In adults, consumption of non-fermented or fermented milk was not significantly associated with incident overweight after 8-12 years of follow-up.</p>	<p><b>Exposure of interest:</b> Non-fermented milk, Fermented milk</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Non-fermented milk intake (categorical; quintiles) <ul style="list-style-type: none"> <li>Q1: Median=0.08 svg/d</li> <li>Q2: Median=0.58 svg/d</li> <li>Q3: Median=1.0 svg/d</li> <li>Q4: Median=1.4 svg/d</li> <li>Q5: Median=2.5 svg/d</li> </ul> </li> <li>Fermented milk intake (categorical; quintiles) <ul style="list-style-type: none"> <li>Q1: Median=0.006 svg/d</li> <li>Q2: Median=0.16 svg/d</li> <li>Q3: Median=0.36 svg/d</li> <li>Q4: Median=0.78 svg/d</li> <li>Q5: Median=1.1 svg/d</li> </ul> </li> </ul> <p>Other exposures: dairy products, cheese, butter</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>FFQ: 84 item version completed by 31% of participants at baseline, and 66 item version completed by 69% of participants at baseline and 100% at follow-up; Represents intake during past year</li> <li>At baseline, 8-12y follow-up</li> </ul> <p><b>Study beverage intake:</b> svg/d</p> <ul style="list-style-type: none"> <li>Non-fermented milk, Mean: ~1.2</li> <li>Total fermented milk, Mean: ~0.6</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 8-12y follow-up</li> <li>Height and weight measured by study personnel</li> <li>Overweight defined as BMI <math>\geq 25</math></li> </ul>	<p><b>Non-fermented milk, categorical Incident overweight</b>, HR (95% CI), Cox proportional hazards regression  By quintile of intake:  Q1 (ref)  Q2: 0.92 (0.80, 1.05)  Q3: 0.95 (0.83, 1.09)  Q4: 1.00 (0.87, 1.15)  Q5: 0.92 (0.79, 1.07)</p> <p><b>Fermented milk, categorical Incident overweight</b>, HR (95% CI), Cox proportional hazards regression  By quintile of intake:  Q1 (ref)  Q2: 1.03 (0.90, 1.18)  Q3: 0.93 (0.81, 1.07)  Q4: 0.91 (0.79, 1.05)  Q5: 0.95 (0.82, 1.10)</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, physical activity, smoking</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, anthropometry at baseline</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Fruit intake, vegetable intake, dairy group</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Start of follow-up and exposure do not coincide</li> <li>FFQ was not validated</li> <li>Attrition 69% with no information on non-completers</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Swedish Research Council for Health, Working Life and Welfare; The Swedish Research Council</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Kaikkonen, 2015<sup>31</sup></b>  <b>Prospective Cohort Study, Young Finns Study, Finland</b>  Baseline N=2276, Analytic N=1715 (Attrition: 25%); Power: NR</p> <p><b>Recruitment:</b> random selection from Finnish national population register</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 53.8%</li> <li>• Age: Mean ~31.7y</li> <li>• Race/ethnicity: NR</li> <li>• SES: Educational status (1=low to 3=high), Mean ~2.11; Occupational status (1=low to 3=high), Mean~1.9</li> <li>• Anthropometrics, Mean (SD): BMI (women), 24.38 (0.149); BMI (men), 25.64 (0.138)</li> <li>• Physical activity: Leisure-time physical activity (5=low to 15=high), Mean ~9.9</li> <li>• Smoking: 23% smoker</li> </ul> <p><b>Summary of findings:</b>  In women, milk intake frequency was not associated with BMI or incident obesity after 6 years. In men, higher milk intake frequency was associated with incident obesity after 6 years and was associated with 6 year weight gain among those who gained at least 2kg.</p>	<p><b>Exposure of interest:</b> Milk</p> <p><b>Comparator:</b> Milk intake (categorical; tertiles)</p> <ul style="list-style-type: none"> <li>• T1 (lowest)</li> <li>• T2</li> <li>• T3 (highest)</li> </ul> <p>Other exposures: sugar-sweetened soft drinks</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Non-quantitative dietary use frequency questionnaire; Represents habitual intake</li> <li>• At baseline (2001; age 24-39y, mean ~32.7y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Milk (1=low, 3=high), mean (SD): Women: 1.76 (0.03), Men: 2.11 (0.03)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 6y follow-up</li> <li>• Height and weight measured by study personnel</li> <li>• Obesity defined as BMI ≥30</li> </ul>	<p><b>BMI, Change over time</b>, linear regression:  <u>Women (n=923):</u>  Not retained in final model; Data NR, P=NS  <b>24-27y (n=265):</b> Not retained in final model; Data NR, P=NS  <b>30-39y (n=658):</b> Not retained in final model; Data NR, P=NS  <b>With weight gain &gt;2kg (n=490):</b> Not retained in final model; Data NR, P=NS</p> <p><u>Men (n=792):</u> Not retained in final model; Data NR, p=NS  <b>24-27y (n=226):</b> Not retained in final model; Data NR, P=NS  <b>30-39y (n=566):</b> Not retained in final model; Data NR, P=NS  <b>With weight gain &gt;2kg (n=455):</b>  <b>Beta=0.126, P=0.0004</b></p> <p><b>Incident obesity</b>, OR (95% CI), logistic regression:  <b>Women (n=823):</b> Not retained in final model; Data NR, P=NS  <b>Men (n=689): 2.20 (1.36, 3.56), P=0.001</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Hormones and inflammatory markers, dietary habits and alcohol use, genetic factors, psychological and childhood factors, living habits and environment</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Dietary questionnaire not validated</li> <li>• Attrition 25% with no information on non-completers</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Academy of Finland; Social Insurance Institution of Finland; Kuopio, Tampere and Turku University Hospital Medical Funds; Yrjo Jahansson Foundation; Juho Vainio Foundation; Paavo Nurmi Foundation; Finnish Foundation of Cardiovascular Research; Finnish Cultural Foundation; Sigrid Juselius Foundation; Tampere Tuberculosis Foundation; Emil Aaltonen Foundation; Signe and Ane Gyllenberg Foundation; Bothnia Welfare Coalition for Research and Knowledge</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Kim, 2017<sup>32</sup></b>  <b>Prospective Cohort Study, Korean Genome and Epidemiology Study, South Korea</b>  Baseline N=10,030, Analytic N=4,702 (Attrition: 53%); Power: NR</p> <p><b>Recruitment:</b> community-based cohort study</p> <p><b>Participant characteristics: adults 40-69y</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean ~1971 kcal/d</li> <li>Sex (female): 48.1%</li> <li>Age: Mean ~51</li> <li>Race/ethnicity: NR</li> <li>SES: Education, ≤6y ~28%, 7-12y ~57%, &gt;12y ~15%</li> <li>Anthropometrics: BMI, Mean ~23.8; WC, Mean ~80.2 cm</li> <li>Physical activity: Mean ~23.5 MET-h/d</li> <li>Smoking: ~56% never, ~17% former, ~27% current</li> </ul> <p><b>Summary of findings:</b>  More frequent milk intake was associated with reduced risk of incident abdominal obesity after ~5.6 years of follow-up in men, but not in women.</p>	<p><b>Exposure of interest:</b> Milk (1 svg=200mL)</p> <p><b>Comparators:</b> Milk intake: categorical; svg/wk (analytic n)</p> <ul style="list-style-type: none"> <li>None (n=1193)</li> <li>&lt;1 (n=1004)</li> <li>1≤ to &lt;4 (n=1388)</li> <li>4≤ to ≤7 (n=926)</li> <li>&gt;7 (n=191)</li> </ul> <p>Other exposures: total dairy, yogurt</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated 103-item semi-quantitative FFQ administered by trained dietitian; Represents usual intake during past year</li> <li>At baseline (~51yo), Second follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Milk (svg/wk): 25%: none, 21%: &lt;1, 30%: 1≤ to &lt;4, 20%: 4≤ to ≤7, 4%: &gt;7</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (2001-02), 4<sup>th</sup> Follow-up (2009-10; Mean~5.6y)</li> <li>Waist circumference measured in triplicate at the narrowest point between lowest rib and iliac crest</li> <li>Abdominal obesity defined as waist circumference ≥90cm in men or ≥80 cm in women</li> </ul>	<p><b>Incident abdominal obesity</b>, HR (95% CI), Cox's proportional hazard  <b>Total, Unadjusted for TEI:</b>  None (ref)  &lt;1: 0.82 (0.63, 1.06)  1≤ to &lt;4: 0.85 (0.67, 1.07)  4≤ to ≤7: 1.21 (0.94, 1.56)  &gt;7: 0.90 (0.55, 1.59), P for trend= 0.4052  <b>Total, Adjusted for TEI:</b>  None (ref)  &lt;1: 0.83 (0.64, 1.08)  1≤ to &lt;4: 0.86 (0.67, 1.09)  4≤ to ≤7: 1.20 (0.92, 1.58)  &gt;7: 0.84 (0.49, 1.44), P for trend= 0.6247</p> <p><b>Men, Unadjusted for TEI:</b>  None (ref)  &lt;1: <b>0.70 (0.57, 0.86)</b>  1≤ to &lt;4: <b>0.79 (0.65, 0.96)</b>  4≤ to ≤7: 0.83 (0.66, 1.04)  &gt;7: 0.76 (0.50, 1.16), P for trend= 0.0999</p> <p><b>Men, Adjusted for TEI:</b>  None (ref)  &lt;1: <b>0.69 (0.56, 0.85)</b>  1≤ to &lt;4: <b>0.76 (0.62, 0.93)</b>  4≤ to ≤7: <b>0.75 (0.58, 0.97)</b>  &gt;7: 0.61 (0.38, 1.00), <b>P for trend= 0.0083</b></p> <p><b>Women, Unadjusted for TEI:</b>  None (ref)  &lt;1: 0.84 (0.66, 1.06)  1≤ to &lt;4: 0.90 (0.74, 1.10)  4≤ to ≤7: 0.84 (0.68, 1.04)  &gt;7: 0.67 (0.44, 1.03), P for trend= 0.0598</p> <p><b>Women, Adjusted for TEI:</b>  None (ref)  &lt;1: 0.84 (0.66, 1.06)  1≤ to &lt;4: 0.90 (0.73, 1.11)  4≤ to ≤7: 0.82 (0.64, 1.04)  &gt;7: 0.64 (0.40, 1.01), P for trend= 0.0717</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Nutrient intakes such as energy-adjusted Ca and fibre (only in TEI adjusted analyses)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Start of follow-up and exposure do not coincide</li> <li>No clear rationale for exposure level category cut-offs (e.g., not quintiles)</li> <li>Attrition 53% without information on non-completers</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Basic Science Research Program of the National Research Foundation of Korea; Ministry of Education, Science, and Technology</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Mozaffarian, 2011</b><sup>42</sup></p> <p><b>Prospective Cohort Study, Nurses Health Study (NHS) + NHS II + Health Professionals Follow-Up Study (HPS), United States</b></p> <p>NHS: Analytic N=50,422 (Attrition: NR); Power: NR  NHS II: Analytic N=47,898 (Attrition: NR) Power: NR  HPS: Analytic N=22,557 (Attrition: NR); Power: NR</p> <p><b>Recruitment:</b> professional organizations or from occupation mailing house lists</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): NHS and NHS II 100%, HPS 0%</li> <li>Age, y, Mean (SD): NHS 52.2 (7.2), NHS II 37.5 (4.1), HPS 50.8 (7.5)</li> <li>Race/ethnicity: primarily white</li> <li>SES: primarily well-educated</li> <li>Anthropometrics, Mean (SD): BMI (kg/m<sup>2</sup>), NHS 23.7 (1.4), NHS II 23.0 (2.7), HPS 24.7 (1.1)</li> <li>Physical activity, MET-hr/wk, Mean (SD): NHS 14.8 (9.9), NHS II 21.6 (25.9), HPS 22.9 (15.1)</li> <li>Smoking: Never smoker 53%, Past smoker 33%, Current smoker 13%, Missing 1%</li> </ul> <p><b>Summary of findings:</b></p> <p>In adults, whole-fat milk intake was not significantly associated with changes in weight over time. However, low-fat milk intake was significantly associated with weight gain in one of the three cohorts, a sample of women.</p>	<p><b>Exposure of interest:</b> Milk intake (skim, low-fat, whole)</p> <p><b>Comparator:</b> Milk intake (continuous; svg/d)</p> <p>Other exposure measures: SSBs, diet soda, fruit juice</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated questionnaire; represents usual dietary intake</li> <li>At baseline, every 4y over 12- to 20-y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Whole milk intake: NR</li> <li>Low-fat milk intake: NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, and every 2y over 12- to 20-y follow-up</li> <li>Weight was collected via self-report from questionnaire</li> </ul>	<p><b>Weight</b>, lb, Linear regression, <math>\beta</math> (95% CI)</p> <p><i>Whole milk</i></p> <p><b>Change per svg/d increase:</b>  NHS: -0.06 (-0.23, 0.11), P=NS  NHS II: 0.00 (-0.29, 0.30), P=NS  HPS: -0.11 (-0.34, 0.12), P=NS</p> <p><i>Low-fat/skim milk</i></p> <p><b>Change per svg/d increase:</b>  NHS: 0.04 (-0.02, 0.05), P=NS  <b>NHS II: 0.21 (0.13, 0.29), P&lt;0.001</b>  HPS: -0.05 (-0.14, 0.03), P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Television watching, sleep duration, dietary variables (fruits, vegetables, whole-fat and low-fat dairy, potato chips, potatoes/fries, whole grains, refined grains, sweets and desserts, processed and unprocessed meats, trans fat, fried foods at and away from home)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Weight was self-reported</li> </ul> <p><b>Funding sources:</b>  NIH; Searle Scholars Program</p>



**Pan, 2013<sup>46</sup>**

**Prospective Cohort Study, Nurses Health Study (NHS) + NHS II + Health Professionals Follow-Up Study (HPS), United States**

NHS: Analytic N=50,013 (Attrition: NR); Power: NR  
NHS II: Analytic N=52,987 (Attrition: NR); Power: NR  
HPS: Analytic N=21,988 (Attrition: NR); Power: NR

**Recruitment:** professional organizations or from occupation mailing house lists

**Participant characteristics: adults**

- Total energy intake: NR
- Sex (female): 82%
- Age: Mean~47y
- Race/ethnicity: primarily white
- SES: primarily well-educated
- Anthropometrics: Overweight 31%, Obesity 17%, BMI: Mean~25 kg/m<sup>2</sup>
- Physical activity: Mean~18 MET-hr/wk
- Smoking: Never smoker 54%, Past smoker 33%, Current smoker 13%

**Summary of findings:**

Neither low-fat milk intake nor whole milk intake was associated with weight change over time in adults. When stratified by baseline BMI status, greater whole milk intake was associated with greater weight gain in individuals with obesity compared to normal weight. When stratified by age and BMI, greater low-fat milk intake was related to greater weight loss over time in older men and men with obesity. However, there were no significant interactions overall between whole milk or low-fat milk intake and weight.

**Exposure of interest:** Milk intake (skim, low-fat, whole)

**Comparator:** Milk intake (continuous; svg/d)

Other exposure measures: water, SSBs, diet beverages, fruit juice, coffee, tea

**Exposure assessment method and timing:**

- Validated FFQ; represents usual intake of foods and beverages
- At baseline, every 4y over 16- to 20-y follow-up

**Study beverage intake:**

- Whole milk intake, svg/d, Mean (5<sup>th</sup>-95<sup>th</sup>): NHS 0.15 (0-1.0), NHS II 0.07 (0-0.43), HPS 0.13 (0-0.79)
- Low-fat milk intake, svg/d, Mean (5<sup>th</sup>-95<sup>th</sup>): NHS 0.76 (0-2.5), NHS II 0.94 (0-2.5), HPS 0.73 (0-2.5)

**Outcome assessment methods/timing:**

- At baseline, and every 2y over 16- to 20-y follow-up
- Weight was collected via self-report from questionnaire

**Weight change over each 4y period**, kg, Linear regression,  $\beta$  (95% CI)

*Whole milk*

**Change per svg/d increase:**

NHS: 0.05 (-0.06, 0.16), P=NR  
NHS II: -0.14 (-0.38, 0.10), P=NR

HPS: 0.03 (-0.11, 0.18), P=NR

**Stratified by age:**  $\leq 50y$ ,  $>50y$

NHS: 0.12 (-0.07, 0.31), 0.09 (-0.05, 0.23), P=0.53

NHS II: -0.09 (-0.34, 0.16), -0.63 (-1.37, 0.11), P=0.68

HPS: 0.10 (-0.12, 0.33), -0.01 (-0.20, 0.18), P=0.11

**Stratified by BMI (kg/m<sup>2</sup>):**  $<25$ , 25-29.9,  $\geq 30$

**NHS: 0.02 (-0.09, 0.12), 0.20 (-0.01, 0.42), 0.05 (-0.38, 0.49), P=0.003**

NHS II: -0.16 (-0.38, 0.06), 0.20 (-0.30, 0.71), -0.42 (-1.20, 0.37), P=0.36

**HPS: -0.14 (-0.30, 0.02), 0.14 (-0.07, 0.35), 0.73 (-0.08, 1.54), P<0.001**

*Low-fat milk*

**Change per svg/d increase:**

NHS: 0.02 (-0.02, 0.05), P=NR

NHS II: 0.09 (0.05, -0.13), P=NR

HPS: -0.03 (-0.08, 0.01), P=NR

**Stratified by age:**  $\leq 50y$ ,  $>50y$

NHS: -0.01 (-0.09, 0.06), 0.16 (0.12, 0.20), P=0.07

NHS II: 0.09 (0.05, 0.13), 0.10 (-0.01, 0.20), P=0.93

**HPS: -0.08 (-0.16, -0.01), -0.01 (-0.07, 0.04), P=0.048**

**Stratified by BMI (kg/m<sup>2</sup>):**  $<25$ , 25-29.9,  $\geq 30$

NHS: 0.01 (-0.02, 0.04), -0.02 (-0.08, 0.04), 0.01 (-0.10, 0.13), P=0.30

NHS II: 0.07 (0.03, 0.11), 0.10 (0.02, 0.17), 0.14 (0.01, 0.26), P=0.22

**HPS: 0.05 (0.00, 0.09), -0.07 (-0.14, -0.01), -0.12 (-0.35, 0.11), P=0.002**

**TEI adjusted:** No

**Confounders accounted for:**

- Key confounders: sex, age, anthropometry at baseline, physical activity, smoking
- Other factors considered: sugar, protein, alcohol

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity, SES
- Other factors considered: total energy intake, timing, temporal use, fiber, energy density, medications, supplements

**Additional model adjustments:**

Television watching, dietary variables (fruits, vegetables, whole grain, refined grain, potatoes, potato chips, red meat, other dairy products, sweets and deserts, nuts, fried foods, and trans fat), other beverage variables

**Limitations:**

- Not all key confounders accounted for
- Weight was self-reported

**Funding source:**

NIH



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Pereira, 2002<sup>47</sup></b>  <b>Prospective Cohort Study, Coronary Artery Risk Development in Young Adults (CARDIA), United States</b>  Baseline N=5115, Analytic N=3157 (Attrition: 38.3%); Power: NR</p> <p><b>Recruitment:</b> telephone, door-to-door</p> <p><b>Participant characteristics: black and white adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 56%</li> <li>• Age: Mean~25.0y</li> <li>• Race/ethnicity: Black 45%, White 55%</li> <li>• SES: Education, Mean~15y</li> <li>• Anthropometrics: BMI: &lt;25 kg/m<sup>2</sup> 71%, ≥25 kg/m<sup>2</sup> 29%</li> <li>• Physical activity: Mean~377 units/d</li> <li>• Smoking: Current smoker 25%</li> </ul> <p><b>Summary of findings:</b>  In black and white adults, when controlling for energy intake, milk and milk drink intake was not significantly associated with risk of obesity 7y later.</p>	<p><b>Exposure of interest:</b> Milk and milk drink intake</p> <p><b>Comparators:</b> Milk intake: 1 daily increment (7/wk)</p> <p>Other exposure measures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated diet history interview; represents usual dietary practices over the past 28d</li> <li>• Weekly frequency of consumption used to estimate relative intake per week</li> <li>• At baseline, 7y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Milk and milk drink intake (times/wk): Blacks, Median~5.0; Whites, Median~8.1</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 7y follow-up</li> <li>• Height measured to nearest 0.5 cm with vertical ruler</li> <li>• Weight measured to nearest 0.2 kg with calibrated balance beam scale</li> <li>• BMI computed as weight in kg divided by height in meters squared</li> <li>• Waist and hips measured to nearest 0.5 cm with tape in duplicate</li> <li>• Waist-hip ratio (WHR) computed from average of 2 values for each measure</li> <li>• Obesity (BMI≥30, or WHR≥0.85 for women and ≥0.90 for men)</li> </ul>	<p><b>Obesity</b>, Logistic regression  Per 1 daily eating occasion among individuals who were overweight at baseline  OR: 0.83, 95% CI: 0.68, 1.00</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: N/A</li> <li>• Other factors considered: timing, temporal use, sugar</li> </ul> <p><b>Additional model adjustments:</b>  Study center, vitamin supplement use, daily caffeine intake, intake frequency of certain foods (whole and refined grains, meat, fruit, vegetables, soda), dietary intake of micronutrients (magnesium, calcium, potassium, and vitamin D)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Baseline and analytic n not clear</li> <li>• Analysis based on eating occasion rather than amount of milk intake</li> <li>• No information on non-completers</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Children's Hospital League; Charles H. Hood Foundation; NIDDK; General Mills, Inc; NHLBI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Rautiainen, 2016<sup>48</sup></b>  <b>Prospective Cohort Study, Women's Health Study (RCT), United States</b>  Baseline N=39,310, Analytic N=18,438 (Attrition: 53.1%); Power: NR</p> <p><b>Recruitment:</b> mail</p> <p><b>Participant characteristics: middle-aged and older adult women</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~1703 kcal/d</li> <li>Sex (female): 100% female</li> <li>Age: Mean~54.5y</li> <li>Race/ethnicity: "predominantly Caucasian"</li> <li>SES: "predominantly health professionals"</li> <li>Anthropometrics: BMI, Mean~22.4 kg/m<sup>2</sup> (inclusion criteria: 18.5-25)</li> <li>Physical activity: Metabolic equivalent task hours per week, Mean~17.0</li> <li>Smoking: Current smokers, 13.8%</li> </ul> <p><b>Summary of findings:</b>  In middle-aged and older adult women, when controlling for energy intake, skim and whole milk intake was not significantly associated with later risk of overweight or obesity.</p>	<p><b>Exposure of interest:</b> Milk intake (skim, whole)</p> <p><b>Comparators:</b> Milk intake (categorical; svg/d):</p> <ul style="list-style-type: none"> <li>0 (ref)</li> <li>&gt;0 to &lt;0.5</li> <li>0.5 to &lt;1</li> <li>≥1</li> </ul> <p>Other exposure measures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents usual dietary intake</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Skim milk intake (svg/d): Mean~0.8; frequency: 0: 17.1%, &gt;0 to &lt;0.5: 34.2%, 0.5 to &lt;1: 8.5%, ≥1: 40.2%</li> <li>Whole milk intake (svg/d): Mean~0.04; frequency: 0: 87.8%, &gt;0 to &lt;0.5: 10.1%, 0.5 to &lt;1: 0.4%, ≥1: 1.7%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, and 2, 3, 5, 6, 9, 11y and annually thereafter until 17y</li> <li>Height and weight: self-reported</li> <li>BMI calculated as weight in kg divided by height in meters squared</li> <li>Weight categories: normal weight (BMI 18.5 to &lt;25), overweight (BMI 25 to &lt;30), obese (BMI≥30)</li> <li>Risk of becoming overweight or obese: from baseline to date of questionnaire on which they first reported overweight or obese, their date of death, or end of follow-up, whichever occurred first</li> </ul>	<p><b>Overweight or Obese (BMI ≥25),</b> HR (95% CI), Cox proportional hazard  <i>Skim Milk (svg/d)</i>  0 (Ref, n=3127)  &gt;0 to &lt;0.5 (n=6248): 1.07 (1.00, 1.14)  0.5 to &lt;1 (n=1545): 1.03 (0.94, 1.13)  ≥1 (n=7344): 1.05 (0.98, 1.12)  P for trend: 0.44</p> <p><i>Whole Milk (svg/d)</i>  0 (Ref, n=15,703)  &gt;0 to &lt;0.5 (n=1808): 0.95 (0.89, 1.03)  0.5 to &lt;1 (n=74): 0.96 (0.68, 1.34)  ≥1 (n=304): 0.88 (0.73, 1.05)  P for trend: 0.14</p>	<p>TEI adjusted: Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, supplements, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications</li> </ul> <p><b>Additional model adjustments:</b>  Randomization treatment, postmenopausal status, hormone replacement therapy, history of hypercholesterolemia, history of hypertension, fruit and vegetable intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Height and weight were self-reported</li> <li>No information on non-completers</li> <li>No preregistered data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding source:</b>  NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Romaguera, 2011<sup>49</sup></b>  <b>Prospective Cohort Study, European Prospective Investigation into Cancer and Nutrition (EPIC); Italy, UK, the Netherlands, Germany, Denmark</b>  Baseline N=102,346, Analytic N=48,631 (Attrition: 52.5%); Power: NR</p> <p><b>Recruitment:</b> invited general population via mail or in person</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 59.5%</li> <li>• Age: 20-60y</li> <li>• Race/ethnicity: Italy 10.4%, UK 12.9%, Netherlands 13.3%, Germany 17.8%, Denmark 45.5%</li> <li>• SES: NR</li> <li>• Anthropometrics: NR</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In men and women, milk intake was associated with lower gain in WC for a given BMI at 5.5y follow-up.</p>	<p><b>Exposure of interest:</b> Milk intake</p> <p><b>Comparator:</b> Milk intake (continuous; 100 kcal/d)</p> <p>Other exposure measures: juice, soft drinks, coffee, tea, and non-alcoholic beverages</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Country-specific validated FFQ; represents usual food intakes</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Milk intake, g/d, Mean (SD): Men, 238.44 (263.06), Range=80.20-364.15; Women, 200.45 (221.19), Range=81.30-332.93</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 5.5y follow-up</li> <li>• Weight and height measured using standard protocol or via self-report</li> <li>• Waist circumference (WC) measured either midway between the lowest rib and iliac crest, at the narrowest torso circumference, or via self-report</li> <li>• BMI calculated as weight (kg) divided by height (m) squared</li> <li>• Waist circumference for a given body mass index (<math>WC_{BMI}</math>) calculated as the residual values from gender- and centre-specific regression equations of WC on BMI using baseline and follow-up values of WC and BMI</li> </ul>	<p><math>\Delta WC_{BMI}</math>, cm/y; Association between milk intake and annual change in WC for given BMI; <math>\beta^2</math> (95% CI), Linear regression</p> <p><b>All: -0.01 (-0.02, -0.00), P=0.005</b>  <b>Men: -0.01 (-0.02, -0.00), P=0.013</b>  <b>Women: -0.02 (-0.03, -0.01), P=0.005</b></p> <p><i>Interaction by gender: P=NS</i></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: N/A</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Follow-up duration, menopausal status and hormone replacement therapy use (in women)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Methods of outcome assessment differed among participants; some data was self-reported</li> <li>• No information on non-completers</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  European Union; Danish Strategic Research Council</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Rosell, 2006</b><sup>50</sup></p> <p><b>Prospective Cohort Study, Swedish Mammography Cohort, Sweden</b></p> <p>Baseline N=38,984, Analytic N=19,352 (Attrition: 50.4%); Power: NR</p> <p><b>Recruitment:</b> invited all women born 1914 to 1948 in central Sweden</p> <p><b>Participant characteristics: perimenopausal women</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~1600kcal/d</li> <li>Sex (female): 100%</li> <li>Age, Mean (SD): 46.3 (4.5) y, Range=40-55</li> <li>Race/ethnicity: NR</li> <li>SES: Education: &lt;10y 63%, 10-12y 10%, &gt;12y 27%</li> <li>Anthropometrics: BMI, Mean=23.7, SD=3.5</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In perimenopausal women, constant intake of <math>\geq 1</math> svg/d of whole milk and sour milk (3% fat) over ~8y was inversely associated with odds for gaining <math>\geq 1</math>kg/y. These findings remained significant for normal weight women but not for women with BMI <math>\geq 25</math>. A decrease in consumption of medium (1.5%) fat milk was associated with lower odds for gaining <math>\geq 1</math>kg/y. There were no significant associations between changes in low fat-milk intake and odds for weight gain.</p>	<p><b>Exposure of interest:</b> Milk intake: whole milk (3% fat), medium-fat milk (1.5%), low-fat milk (<math>\leq 0.5\%</math> fat), whole sour milk (3% fat), low-fat sour milk (0.5%)</p> <p><b>Comparators:</b> Milk intake, change at follow-up (~8.8y) (categorical; svg/d):</p> <ul style="list-style-type: none"> <li>No change, Constant intake of &lt;1 (ref)</li> <li>Increase from &lt;1 to <math>\geq 1</math></li> <li>No change, Constant intake <math>\geq 1</math></li> <li>Decrease from <math>\geq 1</math> to &lt;1</li> </ul> <p>Other exposure measures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents usual intake</li> <li>Baseline, 9y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Whole milk and sour milk, 3% fat (svg/d): &lt;1 69.2%, <math>\geq 1</math> 30.8%</li> <li>Medium-fat milk, 1.5% fat (svg/d): &lt;1 83.2%, <math>\geq 1</math> 16.8%</li> <li>Low-fat milk and sour milk, 0.5% fat (svg/d): &lt;1 63.9%, <math>\geq 1</math> 36.1%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>Baseline, 9y follow-up (mean 8.8y)</li> <li>Body weight was self-reported to the nearest 0.1 kg</li> <li>Mean weight gain <math>\geq 1</math> kg/y calculated as change in weight from baseline to follow-up divided by number of years of follow-up (participants categorized into 2 groups according to mean annual weight change: &lt;1 or <math>\geq 1</math> kg/y)</li> </ul>	<p><b>Whole milk and sour milk, 3% fat</b>  <b>Weight Gain <math>\geq 1</math> kg/yr by change in milk intake (svg/d):</b> OR (95% CI), Logistic regression  No change, &lt;1 (Ref)  Increase &lt;1 to <math>\geq 1</math>: 0.94 (0.82, 1.07)  <b>No change, <math>\geq 1</math>: 0.85 (0.73, 0.99)</b>  Decrease <math>\geq 1</math> to &lt;1: 0.91 (0.79, 1.05)  <b>Whole milk and sour milk*BMI (&lt;25, <math>\geq 25</math>):</b>  <b>p=0.003</b> (Constant intake <math>\geq 1</math> svg/d lower risk of gaining <math>\geq 1</math>kg/y in normal wt women only; Data NR)</p> <p><b>Weight gain:</b> Linear regression, <math>\beta</math>  <b>BMI&lt;25</b>  No change, &lt;1(Ref)  <b>Increase &lt;1 to <math>\geq 1</math>: -0.40, P=0.004</b>  <b>No change, <math>\geq 1</math>: -0.42, P=0.004</b>  <b>Decrease <math>\geq 1</math> to &lt;1: -0.34, P=0.014</b>  <b>BMI<math>\geq 25</math>: P=NS (Data NR)</b></p> <p><b>Medium-fat milk, 1.5% fat</b>  <b>Weight Gain <math>\geq 1</math> kg/yr by change in milk intake (svg/d):</b> OR (95% CI), Logistic regression  No change, &lt;1 (Ref)  Increase &lt;1 to <math>\geq 1</math>: 0.95 (0.82, 1.10)  No change, <math>\geq 1</math>: 0.90 (0.74, 1.10)  <b>Decrease <math>\geq 1</math> to &lt;1: 0.84 (0.72, 0.99)</b>  <b>Medium fat milk* BMI: P=0.016</b></p> <p><b>Low-fat milk and sour milk, 0.5% fat</b>  <b>Weight Gain <math>\geq 1</math> kg/yr by change in milk intake (svg/d):</b> OR (95% CI), Logistic regression  No change, &lt;1 (Ref)  Increase &lt;1 to <math>\geq 1</math>: 1.09 (0.95, 1.24)  No change, <math>\geq 1</math>: 1.03 (0.90, 1.18)  Decrease <math>\geq 1</math> to &lt;1: 1.01 (0.87, 1.18)  <b>Low-fat milk*BMI: P=0.039</b></p>	<p>TEI adjusted: Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, sugar, protein, fiber, supplements, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, physical activity</li> <li>Other factors considered: timing, temporal use, energy density, medications</li> </ul> <p><b>Additional model adjustments:</b>  Parity, calcium intake, conjugated linoleic acid intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Weight was self-reported</li> <li>No information on non-completers</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Swedish Research Council/Longitudinal Studies; The Swedish Cancer Foundation; The Foundation of the Karolinska Institutet</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Shin, 2013<sup>52</sup></b>  <b>Prospective Cohort Study, Anseong and Ansan cohort of the Korean Genome and Epidemiology Study, Korea</b>  Baseline N=10,038, Analytic N=7,240 (Attrition: 27.9%); Power: NR</p> <p><b>Recruitment:</b> random sampling of local telephone directory</p> <p><b>Participant characteristics: middle-aged adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49.9%</li> <li>Age, y: Mean=51.5, Range=40-69</li> <li>Race/ethnicity: NR</li> <li>SES: Education level: Elementary school graduate 28.8%, Middle school graduate 23.5%, High school graduate 33.5%, College graduate or higher 14.2%; Income level (KRW/mo): &lt;1 million 31.6%, 1-1.99 million 30.6%, 2-2.99 million 19.2%, &gt;3 million 18.6%</li> <li>Anthropometrics: BMI, Mean~24.8; Abdominal obesity 25.2%</li> <li>Physical activity: METs/d, Mean~1530.1</li> <li>Smoking: Pack/yr, Mean~6.1</li> </ul> <p><b>Summary of findings:</b>  In middle-aged adults, compared to no milk intake, milk intake ≥7 times/wk was associated with increased risk of abdominal obesity over a 45.5mo follow-up.</p>	<p><b>Exposure of interest:</b> Milk intake (1/2 cup = 100ml)</p> <p><b>Comparator:</b> Milk intake (categorical; times/wk):</p> <ul style="list-style-type: none"> <li>None</li> <li>1</li> <li>2-3</li> <li>4-6</li> <li>≥7</li> </ul> <p>Other exposure measures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents usual intake</li> <li>At baseline, 45.5mo follow-up (IQR 44.4-47.1mo)</li> </ul> <p><b>Study beverage intake:</b>  Milk intake (times/wk):</p> <ul style="list-style-type: none"> <li>None: 36.7%,</li> <li>1: 13.6%,</li> <li>2-3: 14.8%,</li> <li>4-6: 12.9%,</li> <li>≥7: 22.0%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 45.5mo follow-up</li> <li>Waist circumference measured in triplicate by trained health professional</li> <li>Abdominal obesity defined as waist circumference ≥90 cm for men and ≥85 cm for women</li> </ul>	<p><b>Abdominal Obesity</b>, HR (95% CI), Cox proportional hazard  <b>None (Ref, n=2243)</b>  <b>1 time/wk (n=831): 1.01 (0.83, 1.22)</b>  <b>2-3 times/wk (n=953): 1.03 (0.85, 1.25)</b>  <b>4-6 times/wk (n=816): 0.88 (0.71, 1.09)</b>  <b>≥7 times/wk (n=1379): 0.82 (0.68, 0.97)</b>  <b>P for trend: 0.019</b></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Korea Health Industry Development Institute</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Smith, 2015<sup>53</sup></b>  <b>Prospective Cohort Study, Nurses Health Study (NHS) + NHS II + Health Professionals Follow-Up Study (HPS), United States</b>  NHS: Analytic N=46,994 (Attrition: NR); Power: NR  NHS II: Analytic N=47,928 (Attrition: NR); Power: NR  HPS: Analytic N=25,862 (Attrition: NR); Power: NR</p> <p><b>Recruitment:</b> professional organizations or from occupation mailing house lists</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d, Mean (SD): NHS 1805 (244), NHS II 1779 (423), HPS 1980 (279)</li> <li>Sex (female): NHS and NHS II 100%; HPS 0%</li> <li>Age, y, Mean (SD): NHS 48.9 (2.7), NHS II 37.7 (3.2), HPS 47.3 (2.7)</li> <li>Race/ethnicity: Primarily white</li> <li>SES: Primarily educated</li> <li>Anthropometrics, kg/m<sup>2</sup>, Mean (SD): NHS 23.7 (1.4), NHS II 23.0 (2.4), HPS 24.8 (1.1)</li> <li>Physical activity, METs/wk, Mean (SD): NHS 14.9 (9.9), NHS II 21.7 (23.1), HPS 20.7 (13.8)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b> In adult men and women, when controlling for glycemic index, greater low-fat milk intake was significantly associated with greater increases in 4-yr weight change, but whole milk was not.</p>	<p><b>Exposure of interest:</b> Milk intake (whole; low-fat: skim, 1%, 2%); 1 svg=8oz</p> <p><b>Comparator:</b> Milk intake (continuous; svg/d)</p> <p>Other exposure measures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents usual dietary habits</li> <li>At baseline, every 4y over 16- to 24-y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Whole milk intake, svg/d, Mean (SD): NHS 0.15 (0.21), NHS II 0.07 (0.24), HPS 0.14 (0.22)</li> <li>Low-fat milk intake (skim, 1%, &amp; 2%), svg/d, Mean (SD): NHS 0.74 (0.43), NHS II 0.94 (0.79), HPS 0.73 (0.48)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, and every 2y over 16- to 24-y follow-up</li> <li>Weight was collected via self-report from questionnaire; weight change was calculated every 4y</li> </ul>	<p><b>Whole milk</b>  <b>Weight</b>, kg, Linear regression, <math>\beta</math> (95% CI)  <b>4-year change per svg/d increase of whole milk:</b>  <i>Adjusted for glycemic load</i>  NHS: -0.08 (-0.19, 0.03), P=0.16  NHS II: -0.09 (-0.28, 0.10), P=0.36  HPS: 0.08 (-0.07, 0.22), P=0.30  <i>Adjusted for glycemic index</i>  NHS: 0.01 (-0.10, 0.12), P=0.80  NHS II: 0.05 (-0.14, 0.24), P=0.58  HPS: 0.15 (0.00, 0.29), P=0.05  <b>Low-fat milk (skim, 1% and 2%)</b>  <b>Weight</b>, kg, Linear regression, <math>\beta</math> (95% CI)  <b>4-year change per svg/d increase of low-fat milk:</b>  <i>Adjusted for glycemic load</i>  NHS: -0.01 (-0.04, 0.02), P=0.57  NHS II: -0.03 (-0.06, 0.00), P=0.06  HPS: 0.04 (0.00, 0.09), P=0.09  <i>Adjusted for glycemic index</i>  <b>NHS: 0.08 (0.05, 0.11), P&lt;0.0001</b>  <b>NHS II: 0.07 (0.03, 0.10), P&lt;0.0001</b>  <b>HPS: 0.11 (0.06, 0.16), P&lt;0.0001</b></p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, sugar, protein, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Glycemic load, glycemic index, sleep duration, television watching, change in fruit, vegetable, fried foods consumed at home and away from home, trans fats</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Weight was self-reported</li> </ul> <p><b>Funding sources:</b>  Canadian Institutes of Health Research; NHLBI; NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Snijder, 2008</b><sup>54</sup></p> <p><b>Prospective Cohort Study, Hoorn Study, the Netherlands</b></p> <p>Baseline N=1513, Analytic N=1124 (Attrition: 25.7%); Power: NR</p> <p><b>Recruitment:</b> random selection from population register</p> <p><b>Participant characteristics: white older adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: Mean~2090 kcal/d</li> <li>• Sex (female): 54%</li> <li>• Age: Mean~60.0y</li> <li>• Race/ethnicity: 100% white</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI, Mean~26.0</li> <li>• Physical activity: Habitual, Mean~4.3 hr/d; Sports, yes ~33%</li> <li>• Smoking: Yes ~30%</li> </ul> <p><b>Summary of findings:</b></p> <p>In white elderly adults, when controlling for energy intake, there was no significant association between milk intake and weight, BMI, waist circumference, and waist-to-hip ratio at 6.4y follow-up.</p>	<p><b>Exposure of interest:</b> Milk intake (low-fat, skim, and whole; 1 svg = 150 ml)</p> <p><b>Comparator:</b> Milk intake (continuous; svg/d), quartiles</p> <p>Other exposure measures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Semi-quantitative FFQ; represents average food intake</li> <li>• Baseline only</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Milk intake: NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• Baseline, 6.4y follow-up</li> <li>• Weight, height, waist, and hip circumference measured via physical examination</li> <li>• BMI calculated as weight in kilograms divided by height in meters squared</li> <li>• Waist-to-hip ratio calculated as waist circumference divided by hip circumference</li> </ul>	<p><b>Weight</b>, Linear regression P=NS, Data NR</p> <p><b>BMI</b>, Linear regression P=NS, Data NR</p> <p><b>Waist Circumference</b>, Linear regression P=NS, Data NR</p> <p><b>Waist-to-Hip Ratio</b>, Linear regression P=NS, Data NR</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, fiber, medications, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: N/A</li> <li>• Other factors considered: timing, temporal use, sugar, protein, supplements</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Selection bias: participants included in the analyses had lower BMI, WC, and W:H compared to those not included; no diff in dairy consumption</li> <li>• Not generalizable to other racial/ethnic groups</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>Vrije Universiteit Amsterdam; VU University Medical Center; Dutch Diabetes Research Foundation; Dutch Organization for Scientific Research; Netherlands Heart Foundation; Health Research and Development Council of Netherlands; Dutch Dairy Association</p>



**Vergnaud, 2008<sup>56</sup>**

**Prospective Cohort Study,  
Supplementation en Vitamines et  
Minéraux Antioxydants Study (RCT),  
France**

Baseline N=13,017, Analytic N=2267  
(Attrition: 60%); Power: NR

**Recruitment:** national media campaign  
via television, radio, and newspapers

**Participant characteristics: adults**

- Total energy intake, kcal/d, Mean (SD): Men, 2310 (541); Women, 1759 (446)
- Sex (female): 45%
- Age, Mean (SD): Men, 51.5 (4.4) y; Women, 50.8 (4.3) y
- Race/ethnicity: NR
- SES: Education level, Primary 24.0%, Secondary 38.8%, University or equivalent 37.2%
- Anthropometrics, Mean (SD): Men: BMI, 25.2 (3.0) kg/m<sup>2</sup>; Waist, 90.3 (9.0) cm; Women: BMI, 23.5 (3.7); Waist, 76.1 (9.4) cm
- Physical activity: Irregular 23.9%, Low 27.4%, Equivalent to ≥1 hr walking/d 48.7%
- Smoking: Never smoker 49.5%, Previous smoker 40.0%, Current smoker 10.5%

**Summary of findings:**

In overweight men, milk intake was inversely associated with 6y changes in weight and waist circumference. In normal weight men and normal weight and overweight women, there was not a significant association between milk intake and changes in weight or waist circumference over 6 years.

**Exposure of interest:** Milk intake (1 svg = 225 g)

**Comparator:** Milk intake: Quartile 1 (0 svg/d), Quartile 2, Quartile 3, Quartile 4

Other exposure measures: none

**Exposure assessment method and timing:**

- Data from six 24-hr dietary records collected over first 18 mo of 6y follow-up averaged; represents usual daily intake

**Study beverage intake:**

- Milk intake, svg/d, Mean (SD): Men, 0.71 (0.84); Women, 0.65 (0.76)

**Outcome assessment methods/timing:**

- At baseline, 6y follow-up
- Weight measured on electric scale using standardized procedures; change calculated in absolute terms as difference between last and first measure
- Waist circumference (midway between lower ribs and iliac crest) measured using standardized procedures; change calculated in absolute terms as difference between last and first measure

**Weight**, Mean (SE), ANCOVA, svg/d  
**Men, Normal weight at baseline, n=621**

Quartile 1: 1.87 (0.26)  
Quartile 2: 2.01 (0.31)  
Quartile 3: 2.03 (0.30)  
Quartile 4: 2.06 (0.28), P for trend: 0.67

**Men, Overweight at baseline, n=624**

**Quartile 1: 2.47 (0.32)**  
**Quartile 2: 1.86 (0.34)**  
**Quartile 3: 2.22 (0.35)**  
**Quartile 4: 0.98 (0.40), P for trend: 0.02**

**Women, Normal weight at baseline, n=763**

Quartile 1: 1.65 (0.25)  
Quartile 2: 1.69 (0.26)  
Quartile 3: 1.69 (0.26)  
Quartile 4: 2.11 (0.27), P for trend: 0.27

**Women, Overweight at baseline, n=259**

Quartile 1: 0.37 (0.66)  
Quartile 2: 2.76 (0.72)  
Quartile 3: 1.83 (0.70)  
Quartile 4: 2.45 (0.78), P for trend: 0.18

**Waist Circumference**, Mean (SE), ANCOVA, svg/d

**Men, Normal weight at baseline, n=621**

Quartile 1: 0.85 (0.38)  
Quartile 2: 1.92 (0.44)  
Quartile 3: 1.08 (0.43)  
Quartile 4: 1.25 (0.40), P trend: 0.97

**Men, Overweight at baseline, n=624**

**Quartile 1: 1.85 (0.39)**  
**Quartile 2: 0.69 (0.42)**  
**Quartile 3: 1.36 (0.43)**  
**Quartile 4: -0.08 (0.48), P trend: 0.02**

**Women, Normal weight at baseline, n=763**

Quartile 1: 2.56 (0.42)  
Quartile 2: 2.17 (0.45)  
Quartile 3: 2.16 (0.45)  
Quartile 4: 2.17 (0.46), P trend: 0.59

**Women, Overweight at baseline, n=259**

Quartile 1: 0.26 (0.83)  
Quartile 2: 3.20 (0.91)  
Quartile 3: 1.02 (0.87)  
Quartile 4: 3.93 (0.97), P trend: 0.08

**TEI adjusted:** Yes

**Confounders accounted for:**

- Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking
- Other factors considered: total energy intake, supplements, alcohol

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications

**Additional model adjustments:**

Nutritional quality, intervention group, menopausal status (for women), consumption of cheese and yogurt

**Limitations:**

- Not all key confounders accounted for
- Selection bias: participants excluded if they did not complete six 24-hr diet records in first 18mo
- Milk fat level NR
- No preregistered analysis plan

**Funding sources:**

French National Health Ministry



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Wang, 2014<sup>58</sup></b>  <b>Prospective Cohort Study, Framingham Heart Study Offspring Cohort, United States</b>  Baseline N=5124, Analytic N=3440 (Attrition: 33%); Power: NR</p> <p><b>Recruitment:</b> offspring of original Framingham Heart Study cohort</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d, Mean (SD): 1875 (622)</li> <li>Sex (female): 53.6%</li> <li>Age, y, Mean (SD): 54.5 (9.6), Range=26-84</li> <li>Race/ethnicity: mostly Caucasian American of European descent</li> <li>SES: NR</li> <li>Anthropometrics, Mean (SD): BMI (kg/m<sup>2</sup>): 27.4 (4.9); Weight (kg): 77.5 (16.6); Waist circumference (cm): 92.5 (14.2)</li> <li>Physical activity, Mean (SD): Index in metabolic equivalents, 34.9(6.3)</li> <li>Smoking: Regular cigarette smokers 18.6%</li> </ul> <p><b>Summary of findings:</b>  In adults, milk intake was not statistically associated with changes in weight or waist circumference at 13y follow-up.</p>	<p><b>Exposure of interest:</b> Milk intake (skim, low-fat, whole); standardized serving = 8oz glass</p> <p><b>Comparator:</b> Skim/low fat milk intake (svg/wk):</p> <ul style="list-style-type: none"> <li>&lt;1</li> <li>1-&lt;3</li> <li>≥3</li> </ul> <p>Other exposure measures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents average consumption during the past year</li> <li>Baseline, 13y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Skim/low fat milk (svg/wk): Mean=4.83, SD=6.01</li> <li>Frequency of skim/low fat milk (svg/wk): &lt;1: 29.2%; 1≤3: 15.1%; ≥3: 55.7%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>Baseline, 13y follow-up</li> <li>Height and weight measured at a standardized physical examination</li> <li>Waist circumference measured at level of umbilicus underneath gown by a trained professional</li> </ul>	<p><b>Weight:</b> annualized weight change, mean (SE), Repeated-measure regression</p> <ul style="list-style-type: none"> <li>&lt;1 svg/wk (n=2403): 0.13 (0.03)</li> <li>1-&lt;3 svg/wk (n=1248): 0.15 (0.04)</li> <li>≥3 svg/wk (n=4592): 0.16 (0.02)</li> </ul> <p>P for trend: 0.33</p> <p><b>Waist circumference:</b> annualized change, mean (SE), Repeated-measure regression</p> <ul style="list-style-type: none"> <li>&lt;1 svg/wk (n=2403): 0.67 (0.03)</li> <li>1-&lt;3 svg/wk (n=1248): 0.69 (0.04)</li> <li>≥3 svg/wk (n=4592): 0.69 (0.03)</li> </ul> <p>P for trend: 0.53</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, medications</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Overall diet quality, individual food groups, diabetic status, systolic blood pressure, blood lipid profile</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Missing data: Participants who were excluded were older and less healthy</li> <li>No preregistered data analysis plan</li> <li>Racial/ethnic minorities were under-represented in the study sample</li> </ul> <p><b>Funding sources:</b>  NHLBI; USDA; The Dannon Company, Inc.; General Mills Bell Institute of Health and Nutrition</p>

**Table 5: Risk of bias for randomized controlled trials examining milk consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>xi, xii</sup>**

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Barr, 2000 <sup>5</sup>	Some Concerns	Low	Low	Low	Some Concerns
Chee, 2003 <sup>12</sup>	Some Concerns	Low	Some Concerns	Low	Some Concerns
Daly, 2006 <sup>13</sup>	Some Concerns	Low	Low	Low	Low
Faghih, 2011 <sup>19</sup>	Some Concerns	Low	Low	Low	Some Concerns
Fathi, 2016 <sup>20</sup>	Low	Low	Low	Low	Some Concerns
Lee, 2016 <sup>38</sup>	Some Concerns	Low	Low	Low	Low
Wagner, 2007 <sup>57</sup>	Some Concerns	Low	Low	Low	Low

<sup>xi</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xii</sup> Possible ratings of low, some concerns, or high determined using the "[Cochrane Risk-of-bias 2.0](#)" (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). *Cochrane Methods. Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). [dx.doi.org/10.1002/14651858.CD201601](https://doi.org/10.1002/14651858.CD201601).)

**Table 6: Risk of bias for prospective cohort studies examining milk consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>xiii, xiv</sup>**

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Babio, 2015 <sup>4</sup>	Serious	Serious	Low	Low	Moderate	Low	Moderate
Bes-Rastrollo, 2008 <sup>9</sup>	Serious	Low	Moderate	Low	Moderate	Moderate	Moderate
Beydoun, 2018 <sup>10</sup>	Serious	Moderate	Low	Low	Moderate	Low	Moderate
Drapeau, 2004 <sup>16</sup>	Serious	Low	Moderate	Low	Serious	Low	Moderate
Duffey, 2010 <sup>18</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Fresan, 2016 <sup>22</sup>	Serious	Moderate	Low	Low	Low	Moderate	Moderate
Funtikova, 2015 <sup>23</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Guerendiain, 2018 <sup>24</sup>	Serious	Low	Moderate	Low	Serious	Low	Moderate
Guo, 2018 <sup>25</sup>	Serious	Moderate	Low	Low	Moderate	Low	Moderate
Holmberg, 2013 <sup>28</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Johansson, 2018 <sup>30</sup>	Serious	Moderate	Moderate	Low	Moderate	Low	Moderate
Kaikkonen, 2015 <sup>31</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Kim, 2017 <sup>32</sup>	Serious	Moderate	Moderate	Low	Moderate	Low	Moderate
Mozaffarian, 2011 <sup>42</sup>	Serious	Moderate	Low	Low	Low	Serious	Moderate
Pan, 2013 <sup>46</sup>	Serious	Moderate	Low	Low	Low	Serious	Moderate
Pereira, 2002 <sup>47</sup>	Moderate	Low	Moderate	Low	Moderate	Low	Moderate
Rautiainen, 2016 <sup>48</sup>	Serious	Low	Low	Low	Moderate	Serious	Moderate
Romaguera, 2011 <sup>49</sup>	Moderate	Low	Low	Low	Moderate	Moderate	Moderate
Rosell, 2006 <sup>50</sup>	Serious	Low	Low	Low	Moderate	Serious	Moderate
Shin, 2013 <sup>52</sup>	Serious	Moderate	Serious	Low	Moderate	Low	Moderate

<sup>xiii</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xiv</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

Smith, 2015 <sup>53</sup>	Serious	Moderate	Low	Low	Low	Serious	Moderate
Snijder, 2008 <sup>54</sup>	Moderate	Serious	Low	Low	Low	Low	Moderate
Vergnaud, 2008 <sup>56</sup>	Serious	Moderate	Low	Low	Moderate	Moderate	Moderate
Wang, 2014 <sup>58</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Yang, 2017 <sup>60</sup>	No information	No information	No information	No information	No information	No information	Moderate

## BEVERAGE: 100% JUICE

What is the relationship between beverage consumption (100% juice) and growth, size, body composition, and risk of overweight and obesity?

### Conclusion statements and grades

Limited evidence suggests 100% juice intake is not associated with adiposity or height in *children*. (Grade: Limited)

Limited evidence suggests 100% juice consumption is not associated with measures of adiposity in *adults*. (Grade: Limited)

### Summary of the evidence

- 42 articles examined the relationship between 100% juice intake and outcomes related to growth, size, body composition, and risk of overweight or obesity: 23 articles on children and 19 articles on adults.<sup>1,2,7,9,11,15-18,21-23,27,33,34,41-43,46,49,55,61,63-82</sup>  
Studies published between January 2000 and June 2019 were synthesized by age group
  - Children: 23 studies, including 1 RCT and 22 prospective cohort studies
  - Adults: 19 studies, including 4 RCTs, 1 NRCT, and 14 prospective cohort studies
- Evidence in children
  - The 1 RCT and the majority of the higher quality prospective cohort studies found no statistically significant relationship between 100% juice intake and adiposity.
  - The few studies that were significant were not consistent in direction.
  - The evidence in children was limited by lack of clarity in defining the juice exposure; inconsistent quantification of juice consumption, inconsistent measures of adiposity, lack of evidence from stronger study designs, and inadequate adjustment for confounders.
- Evidence in adults
  - The 4 RCTs and 1 NRCT found no statistically significant relationship between 100% juice intake and adiposity.
  - The prospective cohort studies found inconsistent evidence depending on the specific measure of adiposity. For example, roughly half of the studies (n=4) found that greater consumption of 100% juice intake was related to a greater increase in weight, while the others (n=3) found no significant relationship. Studies examining waist circumference were more consistent, with 5 of the 6 studies finding no significant association with 100% juice intake. Further, all studies (n=3) examining body fat or prevalence of (abdominal) obesity found no significant associations with 100% juice intake.
  - The evidence from the RCTs and NRCT were limited by the short durations small sample sizes.
  - The evidence from the prospect cohort studies were limited by the single measurement of the exposure, reliance on self-reported outcome data, inadequate adjustment for confounders, and limited generalizability of the experimental data

## Description of the evidence

Of the 152 articles included in this systematic review, 42 articles were included that address the relationship between 100% juice consumption and outcomes related to growth, size, body composition, and risk of overweight and obesity. The comparator was defined as a different amount (including no intake) of the same beverage type, water, or the solid form of the beverage type (e.g., drinking apple juice compared to eating an apple). The search range included peer-reviewed articles published from January 2000 to June 2019. Studies were included if they were conducted in countries categorized as high or very high on the Human Development Index. Studies with the following designs were included: RCTs, non-randomized controlled trials (NRCTs), prospective and retrospective cohort studies, nested case-control studies, and Mendelian Randomization. Studies were included if the study participants were generally healthy or at risk for chronic disease. Participants ages 2 and above were included. The studies in children and in adults were reviewed and synthesized independently.

### *Study designs:*

- Children: 23 articles (**Table 7**)
  - RCTs: 1 article
  - Prospective cohort studies: 22 articles
- Adults: 19 articles (**Table 10**)
  - RCTs: 4 articles
  - NRCTs: 1 article
  - Prospective cohort studies: 14 articles

## 100% Juice: Children

### ***Population***

The participants ranged in age from 2 to 14 years old at baseline. The RCT enrolled adolescent participants (mean age approximately 14 years). Of the prospective cohort studies, roughly half (n=11) were conducted in younger children age 3-5 years and half were conducted in older children 6-12 years (n=10). A majority of studies enrolled a predominantly non-Hispanic white sample, 6 enrolled >50% minority participants.<sup>34,55,66,67,70,79</sup> The majority of studies were conducted in the United States (n=18) with two conducted in Australia,<sup>1,61</sup> and one study each conducted in the following countries: Canada,<sup>17</sup> Germany,<sup>74</sup> and the UK.<sup>15</sup> Analytic sample sizes ranged from 21 to 15,418.

### ***Intervention/exposure and comparator***

The intervention or exposure of interest for this question was 100% juice, which included 100% fruit juice, 100% vegetable juice, or a combination of the two but did not include juice drinks with added sugars. Eligible comparators included varying levels of 100% juice intake (including no intake or juice diluted with water) and water.

All prospective cohort studies examined varying levels of 100% juice intake as their exposure and comparator of interest. The only study looking at 100% juice compared to water was the RCT.

A small set of studies appeared to examine 100% juice intake as their exposure of interest but did not provide a clear definition, raising the possibility that juice drinks with added sugars may have been included.<sup>41,67,69,82</sup> This was considered a limitation of these studies during evidence synthesis.

## **Outcomes**

To discern 'healthy growth' from 'excessive growth' in children, weight status (prevalence or incidence of overweight or obesity), BMI and BMI z-scores, and body composition measures such as waist circumference and body fat, were considered to reflect "adiposity". To assess 'healthy growth' in children, outcomes such as height and lean mass were considered.

All but two studies in this body of evidence examined either weight or BMI (often as age- and sex-adjusted BMI z-scores) as the primary outcome of interest. Height, waist circumference, percent body fat, and prevalence of overweight were also measured in multiple studies. Most outcome measures were taken by trained study staff, though a small number of studies relied on parent- or self-reported data.<sup>7,17,69</sup>

## **Evidence synthesis**

The majority of studies examining the relationship between 100% juice intake and outcomes related to growth, size, body composition, and risk of overweight and obesity in children found the relationship was not statistically significant.

The RCT enrolled adolescent participants in a six-month resistance training intervention in which they were randomized to consume water or juice (100% orange, apple, or grape) daily to supplement the intervention.<sup>34</sup> There were no significant differences between the juice and water groups at the end of intervention in body mass, fat mass, or fat-free mass in the overall sample. When examined by gender, female adolescents consuming juice daily compared to water had significantly greater fat-free mass at six months.

Of the prospective cohort studies, 12 of the 16 examining weight or BMI (most often as age- and sex-adjusted BMI z-score) found no statistically significant relationship with 100% juice consumption.<sup>1,7,11,15,27,33,43,55,61,66,75,81</sup> In the four studies that found a significant relationship, the direction of association was inconsistent, with two finding a positive relationship<sup>74,79</sup> and two finding a negative.<sup>17,70</sup> Additionally, two of the four found significant associations in subgroup analyses only. Specifically, Guerrero et al<sup>70</sup> found greater 100% juice consumption was significantly associated with more beneficial BMI trajectory from age 4-6 years but only in white participants, and Libuda et al<sup>74</sup> found that greater increase in 100% juice intake was related to greater increase in BMI over five years but only in girls.

Findings from observational studies with other outcomes were also mixed, though most were non-significant. All six studies measuring body fat percentage showed a non-significant relationship with juice intake,<sup>1,21,27,66,74</sup> and two of the three studies examining height also found a non-significant relationship.<sup>2,81</sup>

The studies that did not clearly assess 100% juice intake as the target exposure or intervention (n=4) showed similarly mixed findings.

Energy intake is an important covariate when interpreting studies on the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity because beverages might displace nutrient-dense foods or add additional energy to the diet. Therefore, findings with and without adjustments for energy intake were extracted and reviewed. Conclusion statements reflect the totality and strength of the evidence considering both approaches. Also, funding sources were documented during data extraction for consideration when reviewing this evidence. Further, publication bias is always a consideration; however, it is not a serious concern for this body of evidence because multiple studies reported only non-

significant findings while others reported significant findings or a mix of significant and non-significant. Additionally, there were publications from both very large and small samples.

### **Assessment of the evidence<sup>xv</sup>**

The conclusion statement “evidence suggests 100% juice intake in children is not associated with growth, size, body composition, or risk of overweight or obesity in children” was assigned a grade of **limited**. As outlined and described below, the body of evidence examining 100% juice consumption and growth, size, body composition, and risk of overweight and obesity in children was assessed for the following elements when grading the strength of evidence.

**Consistency:** The majority of studies found a non-significant relationship between 100% juice intake and measures of growth, size, and body composition. The studies that found a significant relationship were inconsistent in both direction of the association and the subgroups showing an effect.

**Directness:** The RCT was designed to directly assess this research question. The prospective cohort studies may have had a broader research objective; however, they still provided adequate data for directly assessing the relationship of interest.

**Precision:** The RCT was adequately powered for the reported analyses; however, many of the observational cohorts enrolled smaller sample sizes.

**Generalizability:** The majority of studies enrolled predominantly white participants, though roughly one third of the observational studies enrolled >50% minority participants. The RCT provides the only data for adolescents, limiting generalizability of these overall conclusions to children from ages roughly 3-12 years.

**Risk of bias:** The prospective cohort studies all failed to adjust for at least one key confounder defined *a priori* in the Analytic Framework, many measured the exposure only once at baseline, multiple provided inadequate information on or adjustment for missing data, and a small number did not adequately define their exposure of interest (see **Table 8** and **Table 9**).

## **100% Juice: Adults**

### **Population**

The majority of studies in adults enrolled a broad age range of participants, often ranging from 18-65 years, though two of the experimental studies and a small number of the observational studies enrolled younger adults only,<sup>18,65,73,77</sup> and four of the observational studies focused specifically on older adults.<sup>68,71,76,78</sup> In studies reporting race/ethnicity data, most enrolled a predominantly white sample. Studies were conducted in a range of high or very high human development index (HDI) countries, including nine in the United States,<sup>9,18,42,46,64,65,72,73,78</sup> three in Spain,<sup>22,23,68</sup> two in Brazil,<sup>63,80</sup> and one each in Canada,<sup>16</sup> Denmark,<sup>71</sup> Iran,<sup>77</sup> and Singapore,<sup>76</sup> and one large, multi-country European cohort.<sup>49</sup> Of the cohort studies, analytic sample sizes ranged from 58 to 52,987.

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<sup>xv</sup> A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.



### ***Intervention/exposure and comparator***

As with children, the intervention or exposure of interest for this question was 100% juice, which included 100% fruit juice, 100% vegetable juice, or a combination of the two but did not include juice drinks with added sugars. The RCTs included a variety of interventions and comparators. One RCT compared orange juice to a usual diet control,<sup>63</sup> one compared grape juice to a usual diet control,<sup>72</sup> another looked at the effect of 100% fruit or vegetable juice compared to consumption of the solid fruit or vegetable in a crossover trial,<sup>73</sup> and the fourth compared tomato juice to water.<sup>77</sup> The NRCT compared reduced-energy cranberry juice (diluted with water) to a usual diet control.<sup>80</sup>

The majority of prospective cohort studies (n=7) examined 100% fruit juice intake as their exposure of interest.<sup>16,18,22,42,46,64,68</sup> Four studies examined both 100% fruit and vegetable juices.<sup>9,23,49,71</sup>

A small set of studies appeared to examine 100% juice intake as their exposure of interest but did not provide a clear definition, raising the possibility that juice drinks with added sweeteners may have been included.<sup>65,76,78</sup> This was considered to be a limitation of these studies during evidence synthesis.

### ***Outcomes***

In adults, weight status (prevalence or incidence of overweight or obesity), BMI, and body composition measures such as waist circumference, body fat, and abdominal adiposity were considered to reflect “adiposity”.

Weight and BMI were the most common outcomes considered in adults and were measured in 14 of the 19 studies with roughly half of these studies relying on self-reported weight and height data.<sup>9,22,42,46,71,76,78</sup> Waist circumference and abdominal obesity were also assessed in multiple studies and were measured by trained study staff in all.

### ***Evidence synthesis***

In parallel with the data in children, most studies examining the association between 100% juice consumption and outcomes related to growth, size, body composition, and risk of overweight and obesity in adults found the relationship was not statistically significant.

This body of evidence included four RCTs, three parallel-arm and one crossover trial, ranging in duration from 20 days to three months. None of the studies found a significant effect of 100% juice intake on BMI or weight change in the full sample; however, one study did find that consuming 100% juice compared to consuming the solid form of the fruit or vegetable resulted in greater weight gain in participants with obesity compared to their lean counterparts.<sup>73</sup> No other outcomes were included consistently across multiple studies.

The NRCT found that daily consumption of 100% cranberry juice diluted with water was not associated with change in BMI or waist circumference over 60 days when compared to a control group that maintained their usual diet.<sup>80</sup>

The 11 prospective cohort studies presented mixed findings. Of the six that examined weight or BMI, three found increased consumption of 100% juice was related to greater weight gain over time, though this was no longer significant when stratified by weight status.<sup>9,42,64</sup> Conversely, a fourth study found a significant relationship but only when results were stratified by baseline weight status.<sup>46</sup>

Six studies examined waist circumference or abdominal obesity and showed more consistent findings. Five of the six studies showed the relationship was not significant,<sup>16,18,23,71</sup> while the sixth showed that 100% juice consumption was related to greater risk of abdominal obesity but only when consuming more than five servings per week.<sup>68</sup>

The three studies that did not clearly assess 100% juice intake as the target exposure or intervention showed similarly mixed findings.<sup>65,76,78</sup>

Energy intake is an important covariate when interpreting studies on the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity because beverages might displace nutrient-dense foods or add additional energy to the diet. Therefore, findings with and without adjustments for energy intake were extracted and reviewed. Conclusion statements reflect the totality and strength of the evidence considering both approaches. Also, funding sources were documented during data extraction for consideration when reviewing this evidence. Further, publication bias is always a consideration; however, it is not a serious concern for this body of evidence because multiple studies reported only non-significant findings while others reported significant findings or a mix of significant and non-significant. Additionally, there were publications from both very large and very small samples.

### **Assessment of the evidence**<sup>xvi</sup>

The conclusion statement “evidence suggests 100% juice consumption is not associated with measures of adiposity in adults” was assigned a grade of **limited**. As outlined and described below, the body of evidence examining 100% juice consumption and growth, size, body composition, and risk of overweight and obesity in adults was assessed for the following elements when grading the strength of evidence.

**Consistency:** the RCT and NRCT data consistently show no association between 100% juice intake and adiposity in adults. The observational data provided consistent data for waist circumference/abdominal obesity but were less consistent for weight and BMI.

**Directness:** The experimental studies were designed to directly assess this research question. The prospective cohort studies often had a broader research objective; however, they still provided adequate data for directly assessing these relationships of interest.

**Precision:** Only one of the five experimental studies provided information on a power analysis, raising the concern of insufficient power in the remaining four. The observational cohorts were large on average, with only one enrolling <1,000 participants, and findings were consistent across different sample sizes.

**Generalizability:** Three of the five experimental studies are conducted in countries where cultural differences may limit generalizability to US populations (Brazil, Iran). Most observational evidence for this question comes from samples of predominantly white adults, and multiple studies enrolled only women, limiting the generalizability to other groups.

**Risk of bias:** Half of the RCTs failed to provide adequate information on their randomization

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<sup>xvi</sup> A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

process, and none provided a preregistered analysis plan (see **Table 11**, **Table 12**, and **Table 13**). For the prospective cohort studies, all but two failed to adjust for at least one key confounder, many relied on self-reported outcome data, many measured the exposure only at baseline and reported high attrition rates, and a small number failed to offer a well-defined exposure of interest.

## **Research recommendations**

To address the limitations of this body of evidence, several research recommendations have been identified:

- Studies examining juice should clearly define their exposure of interest in the measurement tool and in reporting to enable distinction between 100% juices and juice drinks with added sugars.
- Studies examining the relationship between beverage consumption and health outcomes should also compare intake of particular beverages to intake of water
- Trials that give participants a particular beverage as the intervention should give the control group a different beverage to test the effect of substituting one beverage for another

**Table 7: Summary of articles examining the relationship between 100% juice consumption and growth, size, body composition and risk of overweight and obesity in children<sup>xvii</sup>**

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<sup>xvii</sup> Abbreviations: adj: adjusted; ANOVA: analysis of variance; BMI: body mass index; BMI-SDS: BMI standard deviation score; BMIZ: BMI z-score; CDC: Center for Disease Control and Promotion; d: day(s); DXA or DEXA: dual-energy X-ray absorptiometry; FFM: fat-free mass; FFQ: food frequency questionnaire; FM: fat mass; MetSyn: metabolic syndrome; mo: month(s); MZ: monozygotic; N/A: not applicable; NHLBI: National Heart, Lung, and Blood Institute; NIH: National Institutes of Health; NR: not reported; NS: not significant; Ob: obese; OR: odds ratio; Ovwt: overweight; RCT: randomized controlled trial; SD: standard deviation; SE: standard error; SES: socioeconomic status; TEI: total energy intake; unadj; unadjusted; USDA: U.S. Department of Agriculture; WC: waist circumference; WIC: Special Nutrition Program for Women, Infants, and Children; wk: week(s); y: year(s)  
Red and green font indicate significant findings.

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
RANDOMIZED CONTROLLED TRIALS			

**Lambourne, 2013<sup>34</sup>****RCT, United States**

Baseline N=136, Analytic N=108 (Attrition: 21%); Power: Achieved sample size gives 80% power to detect medium difference (Glass's delta = 0.75) in FFM among groups with alpha = 0.05, assuming correlation between repeated measures up to 0.60

**Recruitment:** convenience sample from middle school physical education programs

**Participant characteristics: adolescents participating in resistance training intervention**

- Total energy intake: Mean ~1564 kcal/d
- Sex (female): 64%
- Age: Mean ~13.6y (grades 7-9)
- Race/ethnicity: 86% minorities
- SES: NR
- Anthropometrics: BMI percentile, Mean ~85<sup>th</sup> percentile
- Physical activity: Moderate to vigorous physical activity, Mean ~25 min/d; All participating in resistance training for RCT
- Smoking: NR

**Summary of findings:**

In adolescent girls participating in a resistance training intervention, daily consumption of juice compared to water resulted in greater fat-free mass after 6 months. However, for boys and for girls and boys combined, there was no effect of daily juice consumption compared to water on body mass, fat mass, fat free mass, percent body fat, BMI percentile, or waist circumference.

**Exposure of interest:** Juice (isocaloric amount, compared to milk, of apple, orange, and/or grape juice daily; resistance training 3d/wk), n=34 (Boys, n=14; Girls, n=20)

**Comparator:** Water (24 fl oz/d bottled water; resistance training 3d/wk), n=38 (Boys, n=12; Girls, n=26)

Other interventions: milk

Intervention duration: 6mo

Intervention compliance: Directly observed by study staff on weekdays and obtained by self-report on weekends; Mean (SD) supplements consumed: Milk 83.9% (9.2), Water 89.8% (5.8)

**Study beverage intake:**

- NR

**Outcome assessment methods/timing:**

- At baseline, 6mo
- Height and weight measured by trained research staff
- BMI percentile calculated using CDC software
- Waist circumference measured by trained research staff using procedures of Lohman, Roche, and Martorell (1988)
- Fat Mass (FM), Fat-free mass (FFM), and % body fat: assessed via DXA

**Body mass**, kg, Mean (SD), Linear mixed model

By study group: baseline, 6mo change  
Water: 62.8 (13.8), 2.3 (2.9)  
Juice: 64.8 (11.9), 4.2 (3.1)  
Group, P=0.12; **Time, P<0.0001**

**Boys**

Water: 65.1 (13.8), 2.8 (3.3)  
Juice: 65.9 (11.4), 5.2 (3.1)  
Group, P=0.14; **Time, P<0.0001**

**Girls**

Water: 61.8 (14.0), 2.0 (2.8)  
Juice: 64.1 (12.5), 3.5 (3.1)  
Group, P=0.60; **Time, P<0.0001**

**Fat mass**, kg, Mean (SD), Linear mixed model

By study group: baseline, 6mo change  
Water: 20.9 (10.2), 0.4 (3.6)  
Juice: 20.1 (10.1), 1.6 (2.5)  
Group, P=0.33; **Time, P<0.0001**

**Boys**

Water: 17.4 (10.6), -1.9 (4.7)  
Juice: 16.3 (9.1), 1.2 (2.7)  
Group, P=0.04; Time, P=0.06  
Pairwise comparison, P=NS

**Girls**

Water: 22.5 (9.8), 1.5 (2.5)  
Juice: 22.8 (10.0), 1.9 (2.3)  
Group, P=0.85; **Time, P<0.0001**

**Fat free mass**, kg, Mean (SD), Linear mixed model

By study group: baseline, 6mo change  
Water: 41.4 (8.6), 1.7 (2.9)  
Juice: 44.1 (7.2), 2.7 (1.9)  
Group, P=0.06; **Time, P<0.0001**

**Boys**

Water: 47.9 (9.7), 4.3 (1.4)  
Juice: 49.3 (7.2), 4.0 (1.3)  
Group, P=0.99; **Time, P<0.0001**

**Girls**

**Water: 38.4 (9.7), 0.5 (1.3)**  
**Juice: 40.5 (3.7), 1.8 (1.7)**  
Group, P=0.25; Time, P=0.49  
**Pairwise comparison, P=0.02**

**TEI adjusted:** No

**Energy intake**, kcal/d, Mean

Change by study group:

Control: -16

Juice: 303

**Between groups, P=0.004**

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity
- Other factors considered: none

**Confounders NOT accounted for:**

- Key confounders: SES, smoking
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:**

Study site

**Limitations:**

- No information on randomization and concealment of allocation sequence
- No preregistered analysis plan

**Funding source:**

Dairy Research Institute

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
		<p><b>Percent fat</b>, %, Mean (SD), Linear mixed model  By study group: baseline, 6mo change  Water: 33.5 (11.0), 0 (3.5)  Juice: 31.5 (11.4), 0.4 (2.4)  Group, P=0.99; Time, P=0.05</p> <p><b>Boys</b>  Water: 25.6 (11.0), -2.8 (3.2)  Juice: 24.8 (11.5), 0.0 (2.7)  Group, P=0.05; Time, P=0.87  Pairwise comparison, P=NS</p> <p><b>Girls</b>  Water: 37.2 (11.0), 1.3 (2.9)  Juice: 36.2 (9.0), 0.7 (2.2)  Group, P=0.22; <b>Time, P=0.01</b></p> <p><b>BMI percentile</b>, Mean (SD), Linear mixed model  By study group: baseline, 6mo change  Water: 84.7 (12.7), 0.3 (7.1)  Juice: 85.0 (12.7), 1.5 (4.2)  Group, P=0.56; <b>Time, P&lt;0.0001</b></p> <p><b>Boys</b>  Water: 85.6 (12.7), -2.0 (4.5)  Juice: 85.3 (12.5), 1.5 (4.4)  Group, P=0.07; <b>Time, P=0.04</b></p> <p><b>Girls</b>  Water: 84.3 (12.7), 1.4 (7.9)  Juice: 84.8 (13.2), 1.5 (4.1)  Group, P=0.94; <b>Time, P&lt;0.0001</b></p> <p><b>WC</b>, cm, Mean (SD), Linear mixed model  By study group: baseline, 6mo change  Water: 77.3 (9.3), 0.6 (4.2)  Juice: 76.7 (8.8), 1.7 (2.9)  Group, P=0.20; Time, P=0.67</p> <p><b>Boys</b>  Water: 79.0 (10.3), 0.9 (5.2)  Juice: 78.5 (8.0), 1.3 (3.7)  Group, P=0.21; Time, P=0.85</p> <p><b>Girls</b>  Water: 76.6 (8.9), 0.4 (3.8)  Juice: 75.4 (9.4), 1.9 (2.2)  Group, P=0.25; Time, P=0.49</p>	

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<b>PROSPECTIVE COHORT STUDIES</b>			
<p><b>Berkey, 2004<sup>7</sup></b>  <b>Prospective Cohort Study, Growing Up Today Study, United States</b>            Baseline N=16771, Analytic N=11654 (Attrition: 31%); Power: NR</p> <p><b>Recruitment:</b> convenience sample (children of NHSII participants)</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Boys, Mean~2290 kcal/d; Girls, Mean~2050 kcal/d</li> <li>Sex (female): ~57%</li> <li>Age: Range: 9-14 y</li> <li>Race/ethnicity: White, 94.7%</li> <li>SES: NR</li> <li>Anthropometrics: Overweight (&gt;85<sup>th</sup> percentile CDC BMI charts): boys: 23.2%; girls: 17.5%; Very lean (&lt;10<sup>th</sup> percentile): boys: 7.2%; girls: 8.6%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            There was not a significant association between a change in the number of daily fruit juice servings and change in BMI over 1y in children 9-14 y of age</p>	<p><b>Exposure of interest:</b> Fruit juices (orange juice, apple juice, other juices)</p> <p><b>Comparator:</b> Fruit juice intake (continuous; 1 y change in svg/d)</p> <p>Other exposures: milk, sugar added beverages, diet soda</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Self-administered semi-quantitative, validated FFQ for older children and adolescents; Represents intake during previous year</li> <li>At baseline, 1y follow-up, 2y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Apple juice intake (boys): Mean~0.40 svg/d</li> <li>Orange juice intake (boys): Mean~0.45 svg/d</li> <li>Apple juice intake (girls): Mean~0.41 svg/d</li> <li>Orange juice intake (girls): Mean~0.40 svg/d</li> </ul> <p><b>Outcomes and assessment methods:</b></p> <ul style="list-style-type: none"> <li>At baseline, 1y follow-up, 2y follow-up BMI from height and weight self-reported by children with measuring instructions and suggestion to ask someone for help provided (all have mothers who are nurses in NHSII)</li> </ul>	<p><b>Fruit juice intake, continuous BMI change over 1y</b>, kg/m<sup>2</sup>, <math>\beta</math> (SE), Linear regression            Per 1y svg/d increase:  <b>Not adjusted for TEI</b>            Boys: 0.033 (0.023), P=0.148            Girls: -0.018 (0.020), P=0.361  <b>Adjusted for TEI</b>            Boys: 0.017 (0.024), P=0.488            Girls: -0.021 (0.021), P=0.325</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>            Tanner stage, menarche (girls), height growth, milk type, inactivity, other beverage intake (sugar added, diet soda, fruit juices)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Children lost to follow-up were older and had higher sugar added beverage intake and lower milk intake at baseline</li> <li>Self-reported height and weight</li> <li>Sugar-added beverage analyses differ from analyses for other beverage types</li> <li>No preregistered protocol</li> </ul> <p><b>Funding sources:</b>            NIH; Boston Obesity Nutrition Research Center Grant; CDC; Economic Research Service of the USDA; Kellogg's</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Blum, 2005<sup>11</sup></b>  <b>Prospective Cohort Study, United States</b>  Baseline N=830, Analytic N=166 (Attrition: 80%) Power: NR</p> <p><b>Recruitment:</b> convenience sample of elementary school children in grades 3 through 6 who had participated in a previous study</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake, Mean (SD): 1957.7 (575.3) kcal/d</li> <li>• Sex (female): 55.4%</li> <li>• Age: 9.3 (1.0) y</li> <li>• Race/ethnicity: Caucasian, ~94%</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI z-score, 0.47(1.0); Height, 139.4 (7.9) cm; Weight, 35.7 (8.1) kg</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, juice intake was not associated with BMI z-score two years later.</p>	<p><b>Exposure of interest:</b> 100% juice</p> <p><b>Comparator:</b> 100% juice intake (continuous; oz/d)</p> <p>Other exposures: milk, diet soda, sugar sweetened drinks</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• 24-hr recall with two interviews per 24-hr period; parents of random sub-sample called to verify consumption at home; Represents intake during past 24-hr on school days</li> <li>• At baseline and 2y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• 100% juice (oz/d): Mean=2.1, SD=4.4</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline and 2y follow-up</li> <li>• Weight and height measured</li> <li>• BMI z-score calculated (CDC age and gender specific) from height and weight; Overweight: BMIZ <math>\geq 1.0</math>; Normal weight: BMIZ &lt; 1.0</li> </ul>	<p><b>100% juice intake, continuous</b></p> <p><u>Change in 100% juice intake for Change-in-BMIZ subgroups</u>, oz/d; ANOVA, Mean (SD):</p> <p><b>Unadjusted analysis</b>  Within group differences: (t-tests)  Normal wt at baseline &amp; 2y, n=99: -0.6 (6.4), NS  Overweight at baseline &amp; 2y, n=48: -0.9 (5.6), NS  Gained wt (Normal wt at baseline; Ovwt at 2y), n=11: -0.5 (4.4), NS  Lost wt (Ovwt at baseline; Normal wt at 2y), n=6: 2.3 (5.5), NS  Between group differences (ANOVA): All NS</p> <p><b>BMI z-score</b>, Linear Regression  Increase per oz/d increase in baseline intake:  P=NS, Data: NR</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Change in TEI for Change-in-BMIZ subgroups</b>, kcal/d; ANOVA, Mean (SD):  Within group differences:  Normal wt at baseline &amp; 2y, n=99: -118.4 (724.9), P&lt;0.05  Overweight at baseline &amp; 2y, n=48: -165.1 (693.1), P=NS  Gained wt (Normal wt at baseline; Ovwt at 2y), n=11: -173.6 (592.0), P=NS  Lost wt (Ovwt at baseline; Normal wt at 2y), n=6: 140.3 (920), P=NS  Between group differences: All NS</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline,</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES, physical activity, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Baseline beverage intakes, 2y follow-up beverage intakes</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Single 24-hr recall used to assess intake</li> <li>• Impact of high level of missing data on analyses unclear</li> <li>• No preregistered analysis plan</li> </ul> <p><b>Funding sources:</b> NR</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Carlson, 2012<sup>66</sup></b>  <b>Prospective Cohort Study, MOVE Project (RCT), United States</b>  Baseline N=271, Analytic N=254 (Attrition: 6%); Power: NR</p> <p><b>Recruitment:</b> public recreation centers in San Diego County, California</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 56%</li> <li>• Age, Mean (SD): 6.7 (0.7) y</li> <li>• Race/ethnicity: 48% Latino, 39% non-Hispanic white</li> <li>• SES: Parent had college degree 41%</li> <li>• Anthropometrics: BMI: ≥85<sup>th</sup>% 20%, ≥95<sup>th</sup>% 15%; Body Fat %, Mean (SD)=29.9 (8.7)</li> <li>• Physical activity: 4.35 (2.00) days/wk</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, 100% fruit and vegetable juice intake was not significantly associated changes in BMIZ and percent body fat 2 years later.</p>	<p><b>Exposure of interest:</b> 100% fruit or vegetable juice (svg = 8 oz)</p> <p><b>Comparator:</b> Juice intake (continuous; svg/d)</p> <p>Other exposure measures: SSB</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Unvalidated survey completed by parents; represents usual dietary behavior</li> <li>• At baseline, and 24mo follow-up</li> </ul> <p><b>Study beverage intake:</b> svg/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>• Juice intake: 0.60 (0.56)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, and 24mo follow-up</li> <li>• Height and weight measured by trained staff</li> <li>• Age- and gender-specific BMI percentiles and z-scores (BMIZ) calculated using CDC growth charts</li> <li>• Percent body fat measured using bioelectrical impedance analysis and Schaefer equation</li> </ul>	<p><b>BMIZ</b>, Linear regression, B (95% CI)  <b>Change per svg/d increase:</b>  -0.04 (-0.21, 0.13), P=0.631</p> <p><b>Percent Body Fat</b>, Linear regression, B (95% CI)  <b>Change per svg/d increase:</b>  -1.06 (-2.70, 0.57), P=0.202</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Baseline height</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Exposure measured using unvalidated method</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NIDDK</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Dong, 2015<sup>15</sup></b>  <b>Prospective Cohort Study, Avon Longitudinal Study of Parents and Children (ALSPAC), UK</b>  Baseline N=15444 (recruited), Analytic N=4646 (Attrition: 70%) Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49.2%</li> <li>Age: Mean=7.5y</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI, Mean=16.2; BMI z-score, Mean=0.1</li> <li>Physical activity: Mean=22.9 min/d, SD=15.4 (at 11y)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Among children, neither average intake nor increases in intake of juice over 3y were significantly associated with excessive weight gain (increase in BMI z-score).</p>	<p><b>Exposure of interest:</b> Juices (fruit juices)</p> <p><b>Comparators:</b> Juices (continuous; g/d)</p> <ul style="list-style-type: none"> <li>Per 100 g/d change over 3y</li> <li>Per 100 g/d average across 3y</li> </ul> <p>Other exposures: full-fat milk, low-fat milk, sugar-sweetened beverages, diet soda</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Three-day food diary, child report with help from parent; Represents current intake</li> <li>At 7y, 10y, and 13y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Juices (g/d), Mean (SD): 7y: 94.4 (138.1); 10y: 124.0 (154.7); 13y: 164.7 (208.2)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At 7y, 10y, and 13y</li> <li>Height and weight measured by study personnel</li> <li>Calculated UK age and sex adjusted BMI z-score to represent adiposity</li> <li>Excessive weight gain: increase in adiposity over 3y compared to reference group</li> <li>BMI converted to g for interpretation (assumes 0.01 increase in BMI z-score = 50g)</li> </ul>	<p><b>Excess weight gain (g) over 3y</b>, per 100 g/d increase (change) or per 100 g/d intake (average), Mean, linear regression</p> <p><b>Juice intake, continuous</b>  Change: B: 10, P=NS  Average: B: -15, P=NS  <b>Boys (n=2155)</b>  Change: B: 5, P=NS  <b>Girls (n=2193)</b>  Change: B: 20, P=NS  <b>7-10y period</b>  Change: B: 6, P=NS  <b>10-13y period</b>  Change: B: 25, P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, physical activity</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, anthropometry at baseline, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Puberty status (Tanner stage)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Impact of missing data on analyses unclear</li> <li>Results from subgroup analyses are only report for change data, not average intake data which may show fewer/no significant associations</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NR</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>DuBois, 2016<sup>17</sup></b>  <b>Prospective Cohort Study, Quebec Newborn Twin Study, Canada</b>  Baseline N=1324, Analytic N=304 (Attrition: 77%); Power: NR</p> <p><b>Participant characteristics: monozygotic (MZ) twin children</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean (SD): 1814.37 kcal/d (393.20)</li> <li>Sex (female): 54.6%</li> <li>Age, Mean (SD): 8.96 y (0.56)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics, Mean (SD): BMI, 16.51 (2.50)</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Within MZ twin pairs, there was a negative association between intrapair differences in fruit juice intake at 9y and BMI change from ages 9 to 14.</p>	<p><b>Exposure of interest:</b> Fruit juice</p> <p><b>Comparator:</b> Fruit juice only (kcal), continuous</p> <p>Other exposures: milk, sugary drinks, fruit drinks, soft drinks</p> <p><u>Assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>24-hr recall performed by registered dietitians; Represents usual intake</li> <li>At baseline (9y)</li> </ul> <p><b>Study beverage intake, kcal, Mean (SD)</b></p> <ul style="list-style-type: none"> <li>Fruit juice only: 79.51 (83.26)</li> </ul> <p><b>Outcomes and assessment methods:</b></p> <ul style="list-style-type: none"> <li>At baseline (9y), 12y, 13y, 14y</li> <li>Height and weight self-reported except at baseline (measured)</li> <li>Intrapair difference (MZ twins) in BMI</li> <li>Discordant twins defined as <math>\geq 2</math> BMI units between pairs at least once at 9, 12, 13, and/or 14y</li> <li>Concordant twins defined as <math>&lt; 2</math> BMI units between pairs at all ages</li> </ul>	<p><u><b>Correlation between intrapair differences in intake at 9y (kcal or % energy) and intrapair differences in BMI</b></u> in subsequent yrs; Spearman correlation</p> <p><b>Fruit juice intake, continuous</b>  <b>All: kcal; % energy</b>  12y (n=238): -0.14, NS; -0.15, NS  13y (n=226): <b>-0.17, P&lt;0.05</b>; -0.14, NS  14y (n=212): -0.10, NS; -0.14, NS  <b>Change 9-14y (n=210): -0.21, P&lt;0.05; -0.21, P&lt;0.05</b></p> <p><b>Boys: kcal; % energy</b>  12y (n=102): -0.13, NS; -0.17, NS  13y (n=96): -0.28, NS; -0.24, NS  14y (n=92): -0.24, NS; -0.24, NS  Change 9-14y (n=92): -0.25, NS; -0.23, NS</p> <p><b>Girls: kcal; % energy</b>  12y (n=136): -0.16, NS; -0.13, NS  13y (n=130): -0.11, NS; -0.07, NS  14y (n=120): 0.03, NS; -0.00, NS  Change 9-14y (n=108): -0.18, NS; -0.17, NS</p> <p><b>Refer to paper and supplemental data for additional analyses on:</b></p> <ul style="list-style-type: none"> <li>Comparison of Dietary Intake (at 9 years) Among Leaner and Heavier Twins From Discordant and Concordant MZ Twin Pairs</li> <li>Comparison of Dietary Intake at 9 Years Between Discordant MZ Twins for BMI at 9 Years and Older</li> </ul>	<p><b>TEI adjusted:</b> No</p> <p><b>Correlation between MZ twin pair differences in BMI and TEI (kcal), Spearman correlation</b>  12y: 0.07; 13y: 0.10; 14y: 0.07  Change 9-14y: 0.00</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES,</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Start of follow-up and exposure do not coincide</li> <li>77% attrition with no information on those lost to follow-up</li> <li>Weight and height self-reported</li> <li>No pre-registered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Fonds Quebecois de la Recherche sur la Societe et la Culture; Fonds de la Recherche en Sante du Quebec; Social Science and Humanities Research Council of Canada; National Health Research Development Program; CIHR; Sainte-Justine Hospital Research Centre; Academy of Finland</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Faith, 2006<sup>67</sup></b>  <b>Prospective Cohort Study, United States</b></p> <p>Baseline N=971, Analytic N=825 (Attrition: 15%); Power: NR</p> <p><b>Recruitment:</b> parents of children ages 1-5y recruited from WIC clinics throughout New York state</p> <p><b>Participant characteristics: low-income children participating in WIC</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 47%</li> <li>• Age: 30.2 (9.0) mo</li> <li>• Race/ethnicity: 36% Non-Hispanic White, 21% Non-Hispanic Black, 35% Hispanic, 9% Other</li> <li>• SES, Parent education: 31% &lt;High school, 40% High school, 29% &gt;High school</li> <li>• Anthropometrics: At risk for overweight (&gt;85<sup>th</sup>-94<sup>th</sup> percentile): 15.6%; Overweight (&gt;95<sup>th</sup> percentile): 17.3%</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In a sample of low-income children participating in WIC, increased intake of fruit juice was associated with increased BMI z-score over a follow-up time of 18-48 months. When stratified by baseline weight status, the relationship remained significant for children who were overweight or at risk of overweight at baseline (≥85<sup>th</sup> percentile) but was no longer significant for those &lt;85<sup>th</sup> percentile</p>	<p><b>Exposure of interest:</b> Fruit juice (Not clear if 100% fruit juice) (serving=3/4 cup)</p> <p><b>Comparator:</b> Fruit juice intake (continuous; svg/d)</p> <p>Other exposures measured: Milk</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Non-validated parent-report questionnaire; usual daily intake</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b> svg/d, Mean</p> <ul style="list-style-type: none"> <li>• Fruit juice intake: 3.0</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• Every 6 months for 18-48 months</li> <li>• Weight was measured by WIC staff using a standard balance-beam scale</li> <li>• Height for children &gt;36in tall or &gt;2y measured with stadiometer; otherwise, length was measured using a recumbent board; length converted to height by subtracting 0.5cm</li> <li>• BMI, BMIZ, weight-for-height-Z computed with CDC growth charts</li> <li>• Change in adiposity: defined as change in age- and gender-standardized BMI per month (i.e., BMI z-score slope)</li> <li>• Categorical: ≥85<sup>th</sup> percentile = at risk for overweight or overweight; &lt;85<sup>th</sup> percentile = not at risk or overweight</li> </ul>	<p><b>Change in adiposity per svg/d increase</b>, Multivariate linear regression, <math>\beta</math> (SE)</p> <p><b>Pooled (n=825): 0.005 (0.002), P&lt;0.01</b>  <b>At risk/overwt (n=264): 0.009 (0.003), P&lt;0.01</b>  <b>(Boys showed greater increase than girls, P=0.04; additional data NR)</b>  <b>Not at risk/overwt (n=561): 0.003 (0.002), P=0.13</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, race/ethnicity, anthropometry at baseline</li> <li>• Other factors considered: None</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Food intake, Parental behaviors</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Survey to measure exposure not validated</li> <li>• Exposure definition for juice unclear</li> <li>• Exposure assessed at baseline only</li> <li>• Timing of start of exposure and follow-up may not coincide for all participants</li> <li>• Participants with missing race/ethnicity data excluded; no info on non-completers</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  USDA</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Field, 2003<sup>69</sup></b></p> <p><b>Prospective Cohort Study, Growing Up Today Study, United States</b> Baseline N=16882, Analytic N= 14918; Attrition: 12%; Power: NR</p> <p><b>Recruitment:</b> convenience sample (children of NHSII participants)</p> <p><b>Participant characteristics: preadolescent and adolescent girls and boys</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~2100 kcal/d</li> <li>• Sex (female): 54%</li> <li>• Age: ~12yo (9-14yo)</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI ~19 kg/m<sup>2</sup></li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b> When energy intake was controlled for, there was an association between higher juice intake and increased BMIZ in girls; however, this was not significant when energy was not adjusted for. There was no significant association between juice intake and change in BMIZ for boys.</p>	<p><b>Exposure of interest:</b> Juice (not defined)</p> <p><b>Comparator:</b> Juice intake (continuous; svg/d)</p> <p>Other exposure measures: N/A</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Self-administered semi-quantitative, validated FFQ for older children and adolescents; Represents intake during previous year</li> <li>• At baseline and annually for 3y (1996-1999)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Juice intake: ~0.9 daily servings</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline and annually for 3y (1996-1999)</li> <li>• Height and weight self-reported; BMI calculated</li> <li>• Age- and gender-specific BMI% and BMIZ calculated based on CDC growth charts</li> <li>• Overweight: BMI between the national 85<sup>th</sup> and 95<sup>th</sup> percentile for age and gender</li> <li>• Obese: BMI &gt;95<sup>th</sup> percentile</li> </ul>	<p><b>BMIZ</b>, Annual change: 1996-1999, Conditional linear model, <math>\beta</math> (95%CI)</p> <p><b>Girls:</b> TEI unadj: -0.000 (-0.002, 0.001) <b>TEI adj: 0.003 (0.001, 0.005)</b></p> <p><b>Boys:</b> TEI unadj: 0.000 (-0.002, 0.002) TEI adj: 0.002 (0.000, 0.005)</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, physical activity</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Tanner stage, inactivity</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Exposure (juice) not clearly defined</li> <li>• Self-reported height and weight</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b> CDC; Boston Obesity Nutrition Research Center; NIH; Kellogg Company</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Fiorito, 2009<sup>21</sup></b>  <b>Prospective Cohort Study, United States</b>            Baseline N=197, Analytic N=166 (Attrition: 16%); Power: NR</p> <p><b>Recruitment:</b> Convenience sample via flyers, newspaper advertisements, and mailings/follow-up phone calls</p> <p><b>Participant characteristics: Girls</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 100%</li> <li>• Age: ~5y</li> <li>• Race/ethnicity: Predominantly non-Hispanic white</li> <li>• SES, Mean (SD): Family income, averaged \$50,000-\$75,000; Paternal education, 14.9y (2.7); Maternal education, 14.8y (2.3)</li> <li>• Anthropometrics, Mean (SD): BMI for age percentile, 59.3 (26.6); Body fat %, 20.6 (4.3); Overweight 18%</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            Among girls, fruit juice intake at 5y of age was not significantly associated with body fat percentage through age 15.</p>	<p><b>Exposure of interest:</b> Fruit juice (100% fruit juice); 1 svg=8oz</p> <p><b>Comparator:</b> Fruit juice intake (continuous; 8 oz svg/d)</p> <p>Other exposures: milk, sweetened beverage</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Three, 24-hr recalls (2 weekdays, 1 weekend day) within 2- to 3-wk period conducted by trained staff using NDS-R software and reported by mother; represents usual intake</li> <li>• At baseline (5y of age)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At 7, 9, 11, 13, 15y of age</li> <li>• Body fat % estimated by tricep and subscapular skinfold thickness at age 5, 7, 9, and 11y and DXA scans at age 9, 11, 13 and 15</li> </ul>	<p><b>Body fat percentage.</b> Linear Regression, standardized regression coefficient            7y (N=169): 0.02, P=NS            9y (N=158): 0.02, P=NS            11y (N=164): 0.03, P=NS            13y (N=150): 0.00, P=NS            15y (N=160): -0.02, P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p>Additional model adjustments: N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Reporting bias: not all outcome measures reported for each beverage type</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>            NIH; The National Dairy Council</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Guerrero, 2016</b><sup>70</sup>  <b>Prospective Cohort Study, Early Childhood Longitudinal Study-Birth Cohort (ECLS-B), United States</b>  Baseline N= NR, Analytic N= 15418;  Attrition: NR; Power: NR</p> <p><b>Recruitment:</b> non-probability birth sample was drawn in 2001 for the ECLS-B by the National Center for Education Statistics</p> <p><b>Participant characteristics: young children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 49%</li> <li>• Age: 53 (4.1) mo</li> <li>• Race/ethnicity: 43% White, 16% Black, 11% Asian, 10% Other, 20% Hispanic, 9% Spanish speaking</li> <li>• SES: 79% lived in 2-parent households; ~25% below fed poverty level; Maternal education: 21% High school, 27% College, 31% ≥Bachelor</li> <li>• Anthropometrics: BMI ~16.5; ~33% ovwt or ob</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Juice consumption was not significantly associated with BMI trajectory, except in a subsample of White children.</p>	<p><b>Exposure of interest:</b> 100% Fruit juice intake</p> <p><b>Comparators:</b> 100% Fruit juice intake, categorical:</p> <ul style="list-style-type: none"> <li>• Any intake in the last 7d</li> <li>• No intake in the last 7d</li> </ul> <p>Other exposure measures: soda</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Parental interview: "Was 100% fruit juice consumed in past 7d? Yes/No"</li> <li>• At 48, 60, and 72mo of age</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Any juice last week (age 48mo): ~92%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At 48, 60, and 72mo of age</li> <li>• Height and weight obtained by trained researchers using standardized procedures and equipment</li> <li>• Age- and sex-specific BMI percentiles calculated using 2000 CDC growth charts</li> <li>• Overweight: BMI 85<sup>th</sup>-&lt;95<sup>th</sup>%</li> <li>• Obesity: BMI ≥95%</li> </ul>	<p><b>BMI trajectory over 2y</b>, Hierarchical linear modeling, <math>\beta</math> (SE)  No juice (ref) vs 100% fruit juice within 7d:  -0.101 (0.053), NS</p> <p><i>By race:</i> No juice (ref) vs 100% fruit juice within 7d; <math>\beta</math> (SE)</p> <ul style="list-style-type: none"> <li>• <b>White: -0.142 (0.070), P&lt;0.05</b></li> <li>• Black: -0.082 (0.197), NS</li> <li>• Asian: 0.277 (0.156), NS</li> <li>• Hispanic-English: -0.226 (0.0207), NS</li> <li>• Hispanic-Spanish: -0.021 (0.203), NS</li> </ul>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Birth weight, mother's acculturation, breastfeeding during infancy, soda intake, fast food consumption, daily servings of fruits and vegetables</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Baseline, analytic sample sizes and attrition not clear</li> <li>• Exposure data collection tool not validated</li> <li>• Does not account for amount of exposure (just y/n within 7d)</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  HHS; University of California's Institute of Human Development; McCormick Foundation</p>



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<p><b>Hasnain, 2014<sup>27</sup></b>  <b>Prospective Cohort Study, Framingham Children's Study, USA</b>  Baseline N=106, Analytic N=98 (Attrition: 8%); Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~1724 kcal/d</li> <li>Sex (female): 55.1%</li> <li>Age: 3-5y</li> <li>Race/ethnicity: 100% non-Hispanic white</li> <li>SES: Maternal education &gt;college, ~34%; 100% 2-parent household</li> <li>Anthropometrics: BMI, Mean~16.1</li> <li>Physical activity: Mean~10.7 Caltrac counts/hr</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Greater fruit and vegetable juice intake from 3-9y was associated with a smaller sum of skinfolds and waist circumference at 15-17y; there was no significant association between fruit and vegetable juice intake and body fat % or BMI.</p>	<p><b>Exposure of interest:</b> Fruit and vegetable juice (unsweetened fruit juice, small amounts of vegetable juice and sweetened fruit juice)</p> <p><b>Comparators:</b> Fruit and vegetable juice intake (categorical; tertiles)</p> <ul style="list-style-type: none"> <li>T1 (Mean=1.9 oz/d, SD=1.0)</li> <li>T2 (Mean=4.9 oz/d, SD=1.2)</li> <li>T3 (Mean=10.2 oz/d, SD=2.8)</li> </ul> <p>Other exposures: milk, SSBs, unsweetened/diet beverages</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Up to 4 sets of 3-d diet records annually completed by parents; Represents usual intake</li> <li>At baseline (3-5y), annually for 12y (age 15-17y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Fruit/vegetable juice, Median (5<sup>th</sup>, 95<sup>th</sup> percentile): 5.6 oz/d (0.7, 15.0)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>End of follow-up (15-17y)</li> <li>Weight, height, waist circumference measured by study personnel</li> <li>Four skinfolds (triceps, subscapular, suprailiac, abdominal) measured in duplicate following standard protocol</li> <li>Percent body fat measured with DXA scan</li> </ul>	<p><b>Effects of intake (by tertiles) at ages 3-9y on outcomes at end of follow-up (ages 15-17y);</b> linear regression</p> <p><b>Body fat %</b>, Mean: Data NR, P=0.1199</p> <p><b>BMI</b>, kg/m<sup>2</sup>: Data NR, P=0.0626</p> <p><b>Sum of 4 skinfolds</b>, mm: <b>Data NR, P=0.0383</b></p> <p><b>WC</b>, cm: <b>8cm, P=0.0328</b></p> <p><b>Effects of intake (by tertiles) on sum of skinfolds over time;</b> mixed model</p> <p>T1 vs T2: Data NR, P=0.0984</p> <p><b>T1 vs T3: Data NR, P=0.0001</b></p> <p><b>T2 vs T3: Data NR, P=0.0201</b></p>	<p><b>TEI adjusted:</b> Evaluated but not independent predictor so removed from model</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Percent of calories from fat, mean TV and video time, other beverages consumed, maternal education, maternal BMI</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Validation of 3-d diet records not indicated</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NHLBI; National Dairy Council</p>

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<p><b>Kral, 2008<sup>33</sup></b>  <b>Prospective Cohort Study, United States</b>  Baseline N=NR, Analytic N=49 (Attrition: NR); Power: NR</p> <p><b>Recruitment:</b> convenience sample from newborn nurseries, obstetric practices, pediatric practices and local referrals</p> <p><b>Participant characteristics: children at high or low risk for obesity</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female) at age 3: ~44%</li> <li>• Age: Mean ~3 y</li> <li>• Race/ethnicity: 100% White</li> <li>• SES: NR</li> <li>• Anthropometrics at age 3: BMI z-score, Mean ~ -0.4; WC, Mean ~49.8 cm</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Change in fruit juice intake from 3 to 5y was not significantly associated with change in BMI z-score or WC from 5 to 6y.</p>	<p><b>Exposure of interest:</b> Fruit juice (100% juice)</p> <p><b>Comparator:</b> Fruit juice intake (change from 3y to 5y; continuous; kcal/d)</p> <p>Other exposures: milk, fruit drinks, soda, diet soda, soft drinks, all beverages</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Three day weighed food and beverage record (2 weekdays, 1 weekend day) recorded by primary caregiver; Represents usual intake</li> <li>• At baseline (3y), annually (4y and 5y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Fruit juice: Mean ~8.5 oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, annually (4y, 5y, and 6y)</li> <li>• Waist circumference measured in triplicate at the narrowest part of torso by trained anthropometrists</li> <li>• Height and weight measured in triplicate by trained anthropometrists</li> <li>• BMI z-score calculated using CDC growth charts</li> </ul>	<p><b>BMI z-score change from 5y – 6y</b>, per change in kcal/d from 3y – 5y, B (SE), Linear mixed model:  Data NR, P&gt;0.10</p> <p><b>WC change from 5y – 6y</b>, per change in kcal/d from 3y – 5y, B (SE), Linear mixed model:  Data NR, P=NS</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, race/ethnicity, anthropometry at baseline</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p>Additional model adjustments: N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Exposure data based on parental weighed food records</li> <li>• Baseline n NR; No information to assess risk of bias due to missing data</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH; General Clinical Research Center; Nutrition Center of the Children's Hospital of Philadelphia</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Libuda, 2008<sup>74</sup></b></p> <p><b>Prospective Cohort Study, Dortmund Nutritional and Longitudinally Designed (DONALD), Germany</b> Baseline N=277, Analytic N= 244; Attrition: 12%; Power: NR</p> <p><b>Recruitment:</b> infant recruitment</p> <p><b>Participant characteristics: adolescents</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~8200 kJ</li> <li>• Sex (female): 49%</li> <li>• Age: ~11.9y (9-18y)</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI ~18.3; Body fat: ~19%</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b> In adolescents, fruit juice consumption was not significantly associated with standardized BMI (BMI-SDS) or body fat percentage in boys. An increase in fruit juice intake over 5 years was associated with increased BMI-SDS but not body fat percentage in girls.</p>	<p><b>Exposure of interest:</b> 100% fruit juice</p> <p><b>Comparators:</b> Fruit juice (continuous; g/d)</p> <p>Other exposure measures: regular soft drinks, energetic beverages (combination of fruit juice and soft drinks)</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• 3d weighed dietary records; All foods/bevs before consumption and leftovers were weighed and recorded by the parents or older subjects, on 3 consecutive days; participants chose the 1st day of recording within a given period of time</li> <li>• At baseline and annually for 5y</li> </ul> <p><b>Study beverage intake:</b> g/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>• Fruit juices: Boys: 178 (224), Girls: 180 (236)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline and annually for 5y</li> <li>• Body weight was measured to nearest 0.1 kg using an electronic scale</li> <li>• Height was measured in a standing position to the nearest 0.1 cm using a digital telescopic stadiometer</li> <li>• Skinfold thickness: Triceps and subscapular skinfolds measured on right side of body using skinfold caliper</li> <li>• Body fat percentage (%BF): sum of both skinfolds using equations of Slaughter</li> <li>• Sex- and age-independent BMI standard deviation scores (BMI-SDS) were calculated using the German national reference data</li> <li>• Overweight: BMI values 90<sup>th</sup> – 97<sup>th</sup> percentile of German national reference data</li> <li>• Obesity: BMI values &gt;97<sup>th</sup> percentile</li> </ul>	<p><b>BOYS:</b> <u><b>Association between Fruit Juice (MJ) consumption and BMI-SDS 5y later (β)</b></u> Baseline intake*time: 0.033, P=0.310 Change in intake: -0.002, P=0.964 <u><b>Association between Fruit Juice (MJ) consumption and %BF 5y later (β)</b></u> Baseline intake*time: -0.058, P=0.874 Change in intake: -0.121, P=0.756</p> <p><b>GIRLS:</b> <u><b>Association between Fruit Juice (MJ) consumption and BMI-SDS 5y later (β)</b></u> Baseline intake*time: -0.046, P=0.161 <b>Change in intake: 0.096, P=0.013</b> <u><b>Association between Fruit Juice (MJ) consumption and %BF 5y later (β)</b></u> Baseline intake*time: -0.265, P=0.426 Change in intake: 0.615, P=0.139</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, SES, anthropometry at baseline</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, physical activity, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Time in years after maximal growth velocity (equals years of adolescence) as an indicator for pubertal status, birth weight, maternal BMI</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b> German Federal Ministry of Food, Agriculture and Consumer Protection</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Marshall, 2018<sup>2</sup></b>  <b>Prospective Cohort Study, Iowa Fluoride and Iowa Bone Development Studies, United States</b>  Baseline N=717 Analytic N=571 (Attrition: 20.4%); Power: NR</p> <p><b>Recruitment:</b> at birth</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: at 2-4.7y, Median~1360 kcal/d</li> <li>Sex (female): 51%</li> <li>Age: Range=2-4.7y</li> <li>Race/ethnicity: Non-Hispanic white 94%</li> <li>SES: Mother had 4y college degree 45%, Household annual income ≥\$60,000 19%</li> <li>Anthropometrics: Weight, Mean~20.0 kg; Height, Mean~111.4 cm</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, when controlling for energy intake, juice intake was not significantly associated with changes in height.</p>	<p><b>Exposure of interest:</b> Juice intake (100% juice)</p> <p><b>Comparator:</b> Juice intake (continuous; 8 oz/d)</p> <p>Other exposure measures: milk, SSB, water/other sugar-free beverages</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated beverage frequency questionnaire; represents previous week's beverage intakes</li> <li>At 3- to 6-mo intervals: 2-4.7, 5-8.5, 9-10.5, 11-12.5, 13-14.5, and 15-17y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Juice intake at 2-4.7y: Median ~6.6 oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At ages 5, 9, 11, 13, 15, 17y</li> <li>Height measured without shoes using stadiometer during clinic visits</li> </ul>	<p><b>Height</b>, cm, <b>Change per 8 oz/d increase</b>; Linear regression:  B: 0.32, 95% CI: -0.08, 0.73, P=0.12</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake, protein</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No information on missing data</li> <li>Registry does not contain data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>  NIH; The Roy J. Carver Charitable Trust; Delta Dental of Iowa Foundation</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Marshall, 2019<sup>41</sup></b>  <b>Prospective Cohort Study, Iowa Fluoride and Iowa Bone Development Studies, United States</b>  Baseline N=720 Analytic N=623 (Attrition: 13.5%); Power: NR</p> <p><b>Recruitment:</b> at birth</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: at 2-4.7y, Median~1360 kcal/d</li> <li>Sex (female): 51%</li> <li>Age: Range=2-4.7y</li> <li>Race/ethnicity: Non-Hispanic white 94%</li> <li>SES: Mother had 4y college degree 45%; Household annual income ≥\$60,000 19%; Low 25%, Middle 38%, High 38%</li> <li>Anthropometrics: BMI, Mean~16.0 kg/m<sup>2</sup>; BMIZ, Mean~0.31</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, when controlling for energy intake, juice intake was not significantly associated with changes in BMIZ.</p>	<p><b>Exposure of interest:</b> 100% juice intake (juice drinks were included in this group through age 8.5y, but were assessed separately in later surveys)</p> <p><b>Comparator:</b> Juice intake (continuous; 8 oz/d)</p> <p>Other exposure measures: milk, SSB, water/other sugar-free beverages</p> <p><u><b>Exposure assessment method and timing:</b></u></p> <ul style="list-style-type: none"> <li>Validated beverage frequency questionnaire; represents previous week's beverage intakes</li> <li>At 3- to 6-mo intervals: 2-4.7, 5-8.5, 9-10.5, 11-12.5, 13-14.5, and 15-17y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Juice intake at 2-4.7y: Median~6.6 oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At ages 5, 9, 11, 13, 15, 17y</li> <li>Height measured without shoes using stadiometer during clinic visits</li> <li>Weight was measured at clinic visit using a standard physician's scale</li> <li>BMIs were calculated from weight and height measures (kg/m<sup>2</sup>)</li> <li>Age- and sex-specific BMI z-scores (BMIZ) calculated 2000 CDC growth charts</li> </ul>	<p><b>BMIZ, Change per 8 oz/d increase</b>, Linear regression:  B: -0.001, 95% CI: -0.059, 0.057, P=0.97</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES</li> <li>Other factors considered: total energy intake, protein</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Other beverage intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>100% juice exposure included juice drinks in first 2 assessments</li> <li>No information on missing data</li> <li>Registry does not contain data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>  NIH; The Roy J. Carver Charitable Trust; Delta Dental of Iowa Foundation</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b><u>Mrdjenovic, 2003</u></b><sup>75</sup>  <b>Prospective Cohort Study, Cornell Summer Day Camp (RCT), US</b>  Baseline N=30, Analytic N=21 (Attrition: 30%); Power: NR</p> <p><b>Recruitment:</b> convenience sample</p> <p><b>Participant characteristics: school-aged children participating in intervention</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~1618 kcal/d</li> <li>• Sex (female): 37%</li> <li>• Age: ~8y (6-13y)</li> <li>• Race/ethnicity: mostly white; 17% from minority groups</li> <li>• SES: mostly upper middle-class families</li> <li>• Anthropometrics: BMI ~16.5 kg/m<sup>2</sup></li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In school-aged children enrolled in a summer day camp intervention, fruit juice intake was not significantly associated with weight gain at the end of the intervention.</p>	<p><b>Exposure of interest:</b> Pure or 100% fruit juice</p> <p><b>Comparators:</b> Fruit juice intake (categorical; oz/d):</p> <ul style="list-style-type: none"> <li>• 0 (no drink consumed)</li> <li>• &lt;6 (1 svg/d)</li> <li>• 6-12 (2 glasses or 1 cup)</li> <li>• &gt;12</li> <li>• &gt;16</li> </ul> <p>Other exposure measures: sweetened drinks</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Food consumption at camp (during weekdays) was weighed before and after consumption; food consumption at home (weekend) calculated based on recorded amounts by converting home measures into grams</li> <li>• Children served themselves a drink of their choice whenever they wished, but were requested to report the amounts they drank.</li> <li>• At baseline, 4-8wk follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Fruit juice intake (g/d): Mean~120</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline and during last week of camp (NR)</li> <li>• Height was measured without shoes to the nearest cm with a portable field stadiometer</li> <li>• Weight measured to the nearest gram in the morning before breakfast using portable digital scale</li> <li>• BMI calculated as kg/m<sup>2</sup></li> </ul>	<p><b><u>Weight Gain</u></b>, kg, Multiple regression, <math>\beta</math> (SD)</p> <p><b>Change per oz/d increase:</b>  &lt;6 oz/d: 0.5 (0.4)  6-12 oz/d: Data NR  &gt;12 oz/d: 3.3 (1.95)  &gt;16: Data NR  P for trend=0.2</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Unclear what key confounders were accounted for</li> <li>• Selection bias: not clear why 30 of 42 were selected into study</li> <li>• Amount of beverage consumed self-reported by child</li> <li>• Power analysis NR</li> <li>• Attrition 30%, follow-up time NR</li> <li>• Unclear of outcome assessment timing</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  USDA</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Newby, 2004<sup>43</sup></b>  <b>Prospective Cohort Study, United States</b>            Baseline N=1450, Analytic N=1345            (Attrition: 7%); Power: NR</p> <p><b>Recruitment:</b> WIC clinic, North Dakota</p> <p><b>Participant characteristics: low-income preschool children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~1747 kcal/d</li> <li>Sex (female): 49.8%</li> <li>Age, Mean (SD): 2.9 (0.7) y</li> <li>Race/ethnicity: White 83%, Native American 11%, Other 6%</li> <li>SES: Maternal education, Mean~12.6y; Poverty level: &lt;100%: 55%; 100-133%: 22%; &gt;133-185%: 23%</li> <li>Anthropometrics: BMI, Mean~16.6 kg/m<sup>2</sup>; At risk of overweight 14%, Overweight 6%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            In low-income preschool children, when controlling for energy intake or not, fruit juice intake was not significantly associated with changes in weight or BMI</p>	<p><b>Exposure of interest:</b> Fruit juice intake (100% juice, such as orange and apple)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Fruit juice intake (continuous; oz/d)</li> <li>Fruit juice intake (categorical; oz/d)               <ul style="list-style-type: none"> <li>&lt;12 (ref)</li> <li>≥12</li> </ul> </li> </ul> <p>Other exposure measures: milk, fruit drinks, soda, diet soda</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents dietary intake during previous month</li> <li>At baseline, 6-12mo follow-up (mean 8.4mo)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Fruit juice intake at baseline: Mean~10.7 oz/d; ≥12 oz/d: 45%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 6-12mo follow-up</li> <li>Height measured by trained staff using wall-mounted measuring board</li> <li>Weight measured by trained staff using standard floor-model beam scale</li> <li>Age- and sex-specific BMI calculated based on 2000 CDC growth charts</li> <li>At risk of overweight (BMI 85<sup>th</sup> to &lt;95<sup>th</sup>%); Overweight (BMI≥95<sup>th</sup>%)</li> </ul>	<p><b>Weight</b>, Linear regression  <b>Change per oz/d increase, <math>\beta</math> (SE):</b>            TEI adj: 0.01 (0.01), P=0.23  <b>&lt;12 oz/d (ref) vs. ≥12 oz/d:</b>            NS, Data NR</p> <p><b>BMI</b>, Linear regression  <b>Change per oz/d increase, <math>\beta</math> (SE):</b>            TEI adj: 0.01 (0.00), P=0.20  <b>&lt;12 oz/d (ref) vs. ≥12 oz/d:</b>            NS, Data NR</p> <p>Estimates remained similar when TEI was omitted from model. (Data NR)</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>            Birth weight, other beverages</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Potential selection bias by only including participants with 2 WIC clinic visits 6-12 months apart</li> <li>No preregistered data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>            USDA; NIH Health Harvard Education Program in Cancer Prevention Control; Boston Obesity Nutrition Research Center</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Shefferly, 2016<sup>79</sup></b>  <b>Prospective Cohort Study, Early Childhood Longitudinal Study-Birth Cohort (ECLS-B), United States</b>  Baseline N=10,700, Analytic N=6250 (at 5y); Attrition: 42%) Power: NR</p> <p><b>Recruitment:</b> birth certificates randomly sampled</p> <p><b>Participant characteristics: preschool-aged children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49%</li> <li>Age: 2y</li> <li>Race/ethnicity: White 53.6%, Black 13.7%, Hispanic 25.3%, Asian 2.7%, Other 4.8%</li> <li>SES: High 20.7%, Medium high 20.6%, Medium 20.1%, Medium low 19.7%, Low 18.9%</li> <li>Anthropometrics: Weight status: Normal weight 67.5%, Overweight 15.6%, Obese 16.9%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In preschool-aged children, frequent juice intake at age 2y was significantly associated with greater increases in BMIZ (and lesser increases in height z-score) and higher odds of becoming overweight at age 4y compared to infrequent/non-drinkers.</p>	<p><b>Exposure of interest:</b> 100% fruit juice intake (orange, apple, or grape); 1 svg=8oz</p> <p><b>Comparators:</b> Juice intake (categorical; svg/d):</p> <ul style="list-style-type: none"> <li>Regular drinkers; ≥1</li> <li>Infrequent/non-drinkers; &lt;1</li> </ul> <p>Other exposure measures: none</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Parent interview in the home by trained assessors (or computer at 2y); represents usual intake</li> <li>At baseline (age 2y), age 4y and 5y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Juice intake at baseline (age 2y): 72% were 'regular drinkers' (drank juice at/between meals or snacks)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (age 2y), age 4y and 5y</li> <li>Height and weight obtained by trained researchers using standardized procedures and equipment</li> <li>Age- and sex-specific BMI percentiles and z-scores (BMIZ) calculated using 2000 CDC growth charts</li> <li>Weight categories: normal weight (BMI&lt;85<sup>th</sup>%), overweight (BMI 85<sup>th</sup>-&lt;95<sup>th</sup>%), and obese (BMI≥95<sup>th</sup>%)</li> </ul>	<p><b>Overweight (BMI 85<sup>th</sup>-95<sup>th</sup>%),</b> Logistic regression, OR (95% CI)  <b>Change from 2–4y between groups:</b>  &lt;1 vs ≥1 svg/d: <b>1.30 (1.06, 1.59)</b>  <b>P=0.0129</b></p> <p><b>Change from 4–5y between groups:</b>  &lt;1 vs ≥1 svg/d: 0.86 (0.63, 1.16)  P=0.4010</p> <p><b>Obesity (BMI≥95<sup>th</sup>%),</b> Logistic regression, OR (95% CI)  <b>Change from 2–4y between groups:</b>  &lt;1 vs ≥1 svg/d: 1.30 (0.93, 1.83)  P=0.1293</p> <p><b>Change from 4–5y between groups:</b>  &lt;1 vs ≥1 svg/d: 0.80 (0.43, 1.49)  P=0.4730</p> <p><b>BMIZ,</b> Linear regression, β (SE)  <b>Change from 2–4y between groups:</b>  &lt;1 svg/d: <b>0.030 (0.037)</b>  ≥1 svg/d: <b>0.282 (0.028), P=0.0003</b></p> <p><b>Change from 4–5y between groups:</b>  &lt;1 svg/d: 0.034 (0.031)  ≥1 svg/d: 0.020 (0.021), P=0.6778</p> <p><b>Height z-score,</b> Linear regression, β (SE)  <b>Change from 2–4y between groups:</b>  &lt;1 svg/d: <b>0.410 (0.028)</b>  ≥1 svg/d: <b>0.308 (0.020), P=0.0010</b></p> <p><b>Change from 4–5y between groups:</b>  &lt;1 svg/d: 0.052 (0.020)  ≥1 svg/d: 0.071 (0.015), P=0.3670</p> <p><b>Weight z-score,</b> Linear regression, β (SE)  <b>Change from 2–4y between groups:</b>  &lt;1 svg/d: 0.371 (0.032)  ≥1 svg/d: 0.432 (0.024), P=0.0550</p> <p><b>Change from 4–5y between groups:</b>  &lt;1 svg/d: 0.042 (0.016)  ≥1 svg/d: 0.029 (0.012), P=0.4553</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Maternal BMI</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure data collection tool not validated</li> <li>No information on non-completers</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH; Doris Duke Charitable Foundation Career Development Award</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Skinner, 2001</b><sup>81</sup></p> <p><b>Prospective Cohort Study, United States</b></p> <p>Baseline N=NR, Analytic N=72 (Attrition: NR%); Power: NR</p> <p><b>Recruitment:</b> recruited at age 2-4 months from Southern US (Tennessee)</p> <p><b>Participant characteristics: young children</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d: Mean=1406</li> <li>Sex (female): 49%</li> <li>Age: Mean~27mo</li> <li>Race/ethnicity: 100% white</li> <li>SES: mostly middle or upper SES; all parents except 1 mother had some education beyond high school</li> <li>Anthropometrics: NR</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>Children with higher average 100% juice intake from ages 2y to 6y had (marginally) lower ponderal index at age 72mo. Average juice intake over that period was not significantly associated with changes in height, weight, or BMI.</p>	<p><b>Exposure of interest:</b> 100% juice intake</p> <p><b>Comparator:</b> 100% juice intake (continuous)</p> <p>Other exposure measures: none</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Average of 7 sets of 3-day dietary info (One 24hr recall &amp; 2d food records) from 7 interviews with parent (when child was age ~27, ~34, 42, 48, 54, 60 and 72mo); represents usual intake</li> <li>At baseline (mean age 27mo), and every 6mo until age 72mo</li> </ul> <p><b>Study beverage intake:</b> Mean (SD)</p> <ul style="list-style-type: none"> <li>Juice intake at age 27mo: 6.8 (6.3) oz/d; 0.51 (0.46) oz/kg</li> <li>Juice intake at age 72mo: 3.6 (4.2) oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (age 27mo), and 4y follow-up (age 72mo) <ul style="list-style-type: none"> <li>Growth parameters at 72mo were compared to national norms</li> </ul> </li> <li>Height measured to nearest 0.1 cm by registered dietitian with a steel tape using a wall or doorway and a square</li> <li>Weight measured to nearest 0.1 pound by registered dietitian using standard scale</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>Ponderal index calculated as kg/m<sup>3</sup></li> </ul>	<p><b>Height</b>, cm, General linear model <b>Change per longitudinal juice intake:</b> B=NR; P=0.370</p> <p><b>Weight</b>, kg, General linear model <b>Change per longitudinal juice intake:</b> B=NR; P=0.494</p> <p><b>BMI</b>, kg/m<sup>2</sup>, General linear model <b>Change per longitudinal juice intake:</b> B=-0.057; P=0.099</p> <p><b>Ponderal index</b>, kg/m<sup>3</sup>, General linear model <b>Change per longitudinal juice intake:</b> B=-0.065; P=0.050</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, anthropometry at baseline</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Parent height or body mass index</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No information on baseline sample</li> <li>No information on how missing data were handled (though the amount of missing data was small)</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b> Gerber Products Company; Tennessee Agricultural Experiment Station</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Striegel-Moore, 2006<sup>55*</sup></b>  <b>Prospective Cohort Study, NHLBI Growth and Health Study, United States</b></p> <p>Baseline N=2379 Analytic N=2371 (Attrition: 0.3%); Power: n=1150 per group at 90% power to detect compare change in subscapular skinfold between Black and White girls</p> <p><b>Recruitment:</b> public and parochial schools, local health maintenance organization and Girl Scout troops</p> <p><b>Participant characteristics: adolescent girls</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 100%</li> <li>• Age: Mean ~10y</li> <li>• Race/ethnicity: Black 51%, White 49%</li> <li>• SES: &lt;\$10K: 17%; \$10&lt;20K: 14%; \$20&lt;30K: 15%; \$30&lt;40K: 14%; \$40&lt;50K: 12%; \$50&lt;75K: 17%; ≥\$75K: 6%</li> <li>• Anthropometrics: Weight: ~ 37kg; Height: ~141 cm</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In adolescent girls, fruit juice intake was not significantly associated with changes in BMI at 10y follow-up.</p> <p>* Some info on baseline data and methodology from: Obesity and CVD risk factors in black and white girls: the NHLBI Growth and Health Study. Am J Public Health. 1992; 82:1613-1620.</p>	<p><b>Exposure of interest:</b> 100% fruit juice intake (fruit or vegetable juice bottled, canned, fresh, frozen, sweetened or unsweetened; fruit nectars)</p> <p><b>Comparator:</b> Fruit juice intake (continuous; 100 g/d)</p> <p>Other exposure measures: milk, regular soda, diet soda, fruit drinks, coffee/tea</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated 3-d food records; represents usual intake over 3 consecutive days (2 weekdays and 1 weekend day)</li> <li>• At baseline, and annually for years 1-5, then at years 7, 8, 10</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Fruit juice intake, g/d, Mean (SE): White, 110.46 (4.94); Black, 108.36 (4.86)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• Baseline, annually until 10y follow-up</li> <li>• Weight measured twice by research staff using electronic scale</li> <li>• Height measured twice by research staff using stadiometer</li> <li>• BMI calculated as weight in kilograms divided by height in meters squared</li> </ul>	<p><b>BMI</b>, Linear regression</p> <p><b>Change per 100g/d increase:</b>  B: 0.005, SE: 0.007, P&gt;0.05</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Consumption of other beverage types, site</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Missing data not clearly reported</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NHLBI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Welsh, 2005<sup>82</sup></b>  <b>Prospective Cohort Study, Missouri WIC Program, United States</b>  Baseline N=37421, Analytic N=10904 (Attrition: 71%); Power: NR</p> <p><b>Recruitment:</b> Missouri Pediatric Nutrition Surveillance System (PedNSS)</p> <p><b>Participant characteristics: low-income preschool-aged children</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d: Mean=1780</li> <li>Sex (female): 50.1%</li> <li>Age: Mean=33.8mo</li> <li>Race/ethnicity: White 88.6% Black 5.8%, Other 5.6%</li> <li>SES: all enrolled in Missouri WIC program</li> <li>Anthropometrics: BMI %: Normal or underweight 75.5%, At risk for overweight 14.5%, Overweight 10.1%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In low-income preschool-aged children, when controlling for energy intake, fruit juice intake was significantly associated with increased risk of overweight among children who were overweight at baseline.</p>	<p><b>Exposure of interest:</b> Fruit juice intake (includes vitamin C-containing juices (natural or added), and other juices)—‘other’ may include added sugars; 1 drink=1 parent-defined serving</p> <p><b>Comparators:</b> Fruit juice intake (categorical; drinks/d):</p> <ul style="list-style-type: none"> <li>0-&lt;1 (ref)</li> <li>1-&lt;2</li> <li>2-&lt;3</li> <li>≥3</li> </ul> <p>Other exposure measures: sweet drinks (including and excluding sodas)</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ completed by parents; represents usual intake in the last 4wk</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Vitamin C juice at baseline (drinks/d): 0-&lt;1, 61.0%; 1-&lt;2, 17.6%; 2-&lt;3, 17.7%; ≥3, 3.7%; Mean=1.0 drinks/d</li> <li>Other juice at baseline (drinks/d): 0-&lt;1, 61.9%; 1-&lt;2, 16.8%; 2-&lt;3, 17.7%; ≥3, 3.6%; Other juice: Mean=1.0 drinks/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 1y follow-up</li> <li>Standing height measured using standard measuring board</li> <li>Weight measured using pediatric scale or beam balance scale</li> <li>Age- and sex-specific BMI percentile based on 2000 CDC growth chart</li> <li>Normal or underweight (BMI&lt;85<sup>th</sup>%), at risk for overweight (BMI 85<sup>th</sup>-&lt;95<sup>th</sup>%), overweight (BMI≥95<sup>th</sup>%)</li> </ul>	<p><b>Overweight at follow up (BMI ≥95<sup>th</sup>%),</b> by fruit juice intake (drinks/d) stratified by baseline weight status: Logistic regression, OR (95% CI)</p> <p><i>Normal or underweight at baseline</i>  0-&lt;1 (n=2768, Ref)  1-&lt;2 (n=1815): 1.1 (0.8, 1.5)  2-&lt;3 (n=2210): 1.0 (0.7, 1.4)  ≥3 (n=1435): 1.2 (0.8, 1.7)</p> <p><i>At risk of overweight at baseline</i>  0-&lt;1 (n=573, Ref)  1-&lt;2 (n=345): 1.1 (0.8, 1.6)  2-&lt;3 (n=405): 1.0 (0.7, 1.4)  ≥3 (n=256): 0.8 (0.5, 1.1)</p> <p><i>Overweight at baseline</i>  0-&lt;1 (n=390, Ref)  1-&lt;2 (n=259): 1.5 (1.0, 2.1)  <b>2-&lt;3 (n=262): 1.5 (1.1, 2.2)</b>  ≥3 (n=186): 1.2 (0.8, 1.8)</p>	<p>TEI adjusted: Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, (SES), anthropometry at baseline</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Sweet food intake, high-fat food intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure only measured at baseline</li> <li>Attrition rate unclear, but may be &gt;70%</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NR</p>

**Zheng, 2015<sup>1</sup>****Prospective Cohort Study, Childhood Asthma Prevention Study, Australia**

Baseline N=237 Analytic N=158 (Attrition: 33.3%); Power: NR

**Recruitment:** pregnant women from antenatal clinics

**Participant characteristics: 8yo children**

- Total energy intake: Mean ~8.0 MJ/d
- Sex (female): 48%
- Age: Mean ~8.0y
- Race/ethnicity: Mother born in Australia/New Zealand ~78%; Father born in Australia/New Zealand ~73%
- SES: Maternal education level >12y ~55%; Paternal education level >12y ~58%; Living in disadvantaged area ~20%
- Anthropometrics: BMI z-score, Mean (SD): 0.4(1.0); Overweight/obese 27.2%
- Physical activity: NR
- Smoking: NR
- Intervention group: 54.9%

**Summary of findings:**

In children, 100% fruit juice consumption was not significantly associated with changes in BMIZ or %BF. Using a substitution model, substituting SSBs with 100% fruit juice was not significantly associated with a change in BMIZ or %BF.

**Exposure of interest:** 100% fruit juice intake (apple, blackcurrant, grape, orange, and fruit blend)

**Comparator:** Fruit juice intake (100 g/d) modeled continuously

Other exposure measures: milk, water, SSB, diet drinks, and liquid energy (energy from all beverages)

**Exposure assessment method and timing:**

- Three 24-hr dietary recalls via phone using multiple pass approach completed by children with parental assistance; Represents usual dietary intake on nonconsecutive weekdays and weekends
- At 1y follow-up (age 9y)

**Study beverage intake:**

- Fruit juice intake at baseline (g/d), Mean (SD): ~90(89)

**Outcome assessment methods/timing:**

- Baseline (age 8y), and 3.5y follow-up (age 11.5y)
- Weight measured to nearest 0.1kg
- Height measured using stadiometer
- Age- and sex-specific BMI z-scores (BMIZ) calculated using 2000 CDC growth charts
- Percentage body fat (%BF) measured by bioimpedance analysis

**BMIZ**, Linear regression**Change per 100 g/d increase,  $\beta$  (SE):**

TEI unadj: 0.07 (0.05), P=0.15

TEI adj: 0.07 (0.05), P=0.12

**Change per 100 g/d substitution of SSB,  $\beta$  (SE):**

Bev EI unadj: -0.03 (0.04), P=0.66

Bev EI adj: -0.02 (0.06), P=0.68

**%BF** Linear regression**Change per 100 g/d increase,  $\beta$  (SE):**

TEI unadj: -0.10 (0.45), P=0.84

TEI adj: -0.05 (0.44), P=0.91

**Change per 100 g/d substitution of SSB,  $\beta$  (SE):**

Bev EI unadj: -0.74 (0.65), P=0.26

Bev EI adj: -0.74 (0.66), P=0.26

**TEI adjusted:** Yes and no

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline
- Other factors considered: total energy intake

**Confounders NOT accounted for:**

- Key confounders: physical activity, smoking
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:**

Maternal age at birth, presence of gestational diabetes, exclusive breastfeeding at 3mo, pubertal status, randomization group (omega-3 fatty acid dietary supplementation and house dust mite reduction); Substitution model: EI from non-bev sources

**Limitations:**

- Not all key confounders accounted for
- Anthropometric measures not taken at same time as dietary data
- Exposure data collected at 1 time to represent 3.5y period

**Funding sources:**

National Health and Medical Research Council of Australia; Cooperative Research Centre for Asthma; New South Wales Department of Health; Children's Hospital Westmead

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Zheng, 2015<sup>61</sup></b>  <b>Prospective Cohort Study, European Youth Heart Study (EYHS), Denmark</b>  Baseline N=590, Analytic N=358 (Attrition: 39%); Power: NR</p> <p><b>Recruitment:</b> schools in Odense, Denmark</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: 9.1 (2.3) MJ/d</li> <li>Sex (female): 56%</li> <li>Age: 9.6 (0.4) y</li> <li>Race/ethnicity: NR</li> <li>SES: 47% Low (elementary, high school, or vocational education)</li> <li>Anthropometrics: BMI 17.2 (2.3) kg/m<sup>2</sup>; BMI z-score 0.4 (1.1)</li> <li>Physical activity: 55% Active (regular exercise)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, 100% fruit juice intake was not significantly associated with changes in BMI, waist circumference, or skinfold measurements at 6y follow-up.</p>	<p><b>Exposure of interest:</b> 100% pure fruit juice intake (apple, orange, or other juice)</p> <p><b>Comparator:</b> Fruit juice intake (100g/d) modeled continuously</p> <p>Other exposure measures: water, SSB, milk, coffee/tea</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>One 24h recall face-to-face interview supplemented with parent-assisted food record; represents food intake</li> <li>At baseline (age 9)</li> </ul> <p><b>Study beverage intake:</b> g/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>Fruit juice intake: 62.4 (139.0)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (age 9), and 6y follow-up (age 15)</li> <li>Height measured bare feet to nearest 5mm using stadiometer</li> <li>Weight measured to nearest 0.1 kg using beam balance scale</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>Age- and sex-specific BMI z-score (BMIZ) generated using the least mean squares method</li> <li>Waist circumference (WC) measured twice with metal anthropometric tape (mean was used)</li> <li>Sum of 4 skinfolds (<math>\Sigma</math>4SF) obtained by adding average skinfolds of 4 sites (biceps, triceps, subscapular, and suprailiac) that were measured in duplicate with Harpenden fat calipers</li> </ul>	<p><i>Base Model</i> (Model 1 in paper) adjusted for confounders listed to the right, but did not adjust for TEI</p> <p><i>Standard Multivariate Model</i> (Model 2 in paper) adjusted for TEI</p> <p><i>Energy Partition Model</i> (Model 3 in paper) included energy-containing beverages only (ie, excluded water) and adjusted for energy from non-beverage sources.</p> <p><b>Change in BMI age 9-15y:</b> kg/m<sup>2</sup>, Per 100 g/d increase, Linear regression, <math>\beta</math> (SE)  Base Model: 0.02 (0.03), P=0.39  TEI Model: 0.03 (0.03), P=0.34  Energy Partition: 0.03 (0.03), P=0.35</p> <p><b>Change in WC age 9-15y:</b> Per 100 g/d increase, Linear regression, <math>\beta</math> (SE)  Base Model: -0.01 (0.22), P=0.59  TEI Model: -0.01 (0.23), P=0.96  Energy Partition: -0.01 (0.22), P=0.95</p> <p><b>Change in <math>\Sigma</math>4SF age 9-15y:</b> mm, Per 100 g/d increase, Linear regression, <math>\beta</math> (SE)  Base Model: 0.47 (0.54), P=0.38  TEI Model: 0.58 (0.57), P=0.31  Energy Partition: 0.60 (0.56), P=0.28</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Pubertal status, Sex x SES, individual beverage intakes, energy from non-beverage sources</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure only measured once (at baseline)</li> <li>Exposure measured with single 24h dietary recall—may not reflect habitual intake</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NR</p>

**Table 8: Risk of bias for the randomized controlled trial examining 100% juice consumption and growth, size, body composition and risk of overweight and obesity in children<sup>xviii, xix</sup>**

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Lambourne, 2013 <sup>34</sup>	Some Concerns	Low	Low	Low	Some Concerns

<sup>xviii</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xix</sup> Possible ratings of low, some concerns, or high determined using the "[Cochrane Risk-of-bias 2.0](#)" (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). *Cochrane Methods. Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). [dx.doi.org/10.1002/14651858.CD201601](https://doi.org/10.1002/14651858.CD201601).)

**Table 9. Risk of bias for prospective cohort studies examining 100% juice consumption and growth, size, body composition and risk of overweight and obesity in children<sup>xx, xxi</sup>**

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Berkey, 2004 <sup>7</sup>	Serious	Low	Low	Low	Moderate	Moderate	Serious
Blum, 2005 <sup>11</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Carlson, 2012 <sup>66</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Dong, 2015 <sup>15</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Dubois, 2016 <sup>17</sup>	Serious	Low	Low	Low	Moderate	Moderate	Moderate
Faith, 2006 <sup>67</sup>	Serious	Moderate	Moderate	Moderate	Moderate	Low	Moderate
Field, 2003 <sup>69</sup>	Serious	Low	Low	Low	Low	Moderate	Moderate
Fiorito, 2009 <sup>21</sup>	Serious	Low	Low	Low	Low	Low	Serious
Guerrero, 2016 <sup>70</sup>	Serious	Low	Serious	Low	Moderate	Low	Moderate
Hasnain, 2014 <sup>27</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Kral, 2008 <sup>33</sup>	Serious	Low	Moderate	Low	No information	Low	Moderate
Libuda, 2008 <sup>74</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Marshall, 2018 <sup>2</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Marshall, 2019 <sup>41</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Mrdjenovic, 2003 <sup>75</sup>	Serious	Serious	Moderate	Low	Low	Low	Moderate
Newby, 2004 <sup>43</sup>	Serious	Moderate	Low	Low	Low	Low	Moderate
Shefferly, 2016 <sup>79</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Skinner, 2001 <sup>81</sup>	Serious	Moderate	Low	Low	Moderate	Low	Moderate
Striegel-Moore, 2006 <sup>55</sup>	Serious	Low	Low	Low	No information	Low	Moderate

<sup>xx</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xxi</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

Welsh, 2005 <sup>82</sup>	Serious	Low	Low	Moderate	Low	Low	Moderate
Zheng, 2015 <sup>1</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Zheng, 2015 <sup>61</sup>	Serious	Low	Moderate	Moderate	Low	Low	Moderate



**Table 10: Summary of articles examining relationship between 100% juice consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>xxii</sup>**

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
CONTROLLED TRIALS			

<sup>xxii</sup> Abbreviations: adj: adjusted; BMI: body mass index; CGJ: Concord grape juice; CI: confidence interval; FFQ: food frequency questionnaire; NHLBI: National Heart, Lung, and Blood Institute; NIH: National Institutes of Health; NA: not applicable; NR: not reported; NS: not significant; OJ: orange juice; OR: odds ratio; RCT: randomized controlled trial; RR: relative risk; SD: standard deviation; SEM: standard error of the mean; SES: socioeconomic status; TEI: total energy intake; unadj: unadjusted; WC: waist circumference  
 Red font indicates a statistically significant detrimental relationship, and green font indicates a statistically significant beneficial relationship.

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Aptekmann, 2010</b><sup>63</sup>  <b>RCT, Brazil</b>  Baseline N=30, Analytic N=26 (Attrition: 13%); Power: NR</p> <p><b>Recruitment:</b> advertisement in local TV and radio stations of the city of Matao, SP, Brazil</p> <p><b>Participant characteristics: overweight or obese women</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~8 MJ, NS</li> <li>• Sex (female): 100%</li> <li>• Age: 30-48yo</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: 37% overweight, 63% obese; Weight: 75.5 (14.2) kg</li> <li>• Physical activity: all "sedentary", NS</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  After a 3-mo intervention where women who were overweight or had obesity participated in regular aerobic exercise, there was no difference in weight, BMI, body fat, or skinfold thickness between women who drank 500mL/d orange juice and those who did not.</p>	<p><b>Intervention:</b> Orange juice (500 mL/d); plus 1h aerobic training sessions 3d/wk, n=13</p> <p><b>Comparator:</b> Usual intake (little/no OJ); plus 1h aerobic training sessions 3d/wk, n=13</p> <p><b>Intervention duration:</b> 3mo</p> <p><b>Intervention compliance:</b> verified indirectly by self-report; all confirmed they drank the preset amount of orange juice daily</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Inclusion criteria: irregular or no consumption of OJ</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• 1<sup>st</sup> and 90<sup>th</sup> day</li> <li>• Weight and height measured, BMI calculated</li> <li>• Body fat (%): assessed early in the morning with a bioelectrical impedance device before the participants broke the overnight fast or exercised</li> <li>• Skinfold thickness: Triceps, abdominal and thigh skinfold thicknesses were measured three times with a Lange Skinfold Caliper (Cambridge Scientific Industries, Inc.), average was used as the reference value</li> </ul>	<p><b>Weight</b>, kg, Paired t-test, Mean (SD)  Within group, over time: before, after Control: 76.3(15.3), 74.5(15.9), P&lt;0.05  OJ: 74.6 (13.0), 73.6 (12.4), P&lt;0.05  Between groups, at follow-up: NS</p> <p><b>BMI</b>, kg/m<sup>2</sup>, Paired t-test, Mean (SD)  Within group, over time: before, after Control: 29.0(5.53), 28.3(5.81), P&lt;0.05  OJ: 28.4 (4.46), 28.1 (4.47), P&lt;0.05  Between groups, at follow-up: NS</p> <p><b>Body fat (%)</b>, Paired t-test, Mean (SD)  Within group, over time: before, after Control: 39.3 (7.33), 33.8 (7.98), P&lt;0.05  OJ: 37.7 (7.56), 33.4 (7.42), P&lt;0.05  Between groups, at follow-up: NS</p> <p><b>Skinfold thickness</b>, mm, Mean (SD)  <i>Tricep</i>  Within group, over time: before, after Control: 32.0 (10.1), 27.3 (9.33), P&lt;0.05  OJ: 31.9 (7.90), 26.6 (6.85), P&lt;0.05  Between groups, at follow-up: NS  <i>Abdominal</i>  Within group, over time: before, after Control: 30.2 (14.3), 25.5 (11.9), P&lt;0.05  OJ: 32.2 (11.8), 29.3 (9.60), P&lt;0.05  Between groups, at follow-up: NS  <i>Thigh</i>  Within group, over time: before, after Control: 53.0 (12.8), 45.9 (14.9), P&lt;0.05  OJ: 52.6 (11.5), 43.4 (9.99), P&lt;0.05  Between groups, at follow-up: NS</p>	<p><b>TEI adjusted:</b> No (NS btwn groups)</p> <p><b>Energy intake</b>, MJ, Mean (SD)  Within group, over time: before, after Control: 7.85 (1.90), 7.70 (1.32), NS  OJ: 8.48 (2.09), 8.04 (1.97), NS  Between groups, at follow-up: NS</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, physical activity</li> <li>• Other factors considered: total energy intake (NS), protein (NS), medications, supplements</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, race/ethnicity, SES, anthropometry at baseline, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, fiber, energy density, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Nutrient intake (carbohydrate, total fat, SFA, PUFA, MUFA, Vitamin C, folate) and cholesterol (all NS)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Randomization and allocation methods NR</li> <li>• Not all key confounders accounted for</li> <li>• No power calculation</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Fischer Group; "Associação Laranja Brasil"</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Hollis, 2009<sup>72</sup></b>  <b>RCT, US</b>  Baseline N=86, Analytic N= 76; Attrition: 12%; Power: NR</p> <p><b>Recruitment:</b> NR</p> <p><b>Participant characteristics: overweight adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: ~8860 kJ</li> <li>Sex (female): NR</li> <li>Age:18-50y, Mean ~25y (P&lt;0.05, between grps)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI ~27, NS</li> <li>Physical activity: NR</li> <li>Smoking: 100% nonsmokers (inclusion criteria: no use of tobacco products)</li> </ul> <p><b>Summary of findings:</b>  Compared to a “no treatment” control group, adults who consumed Concord grape juice (480 mL/d for 12wk) did not differ in weight, BMI, or waist circumference.</p>	<p><b>Intervention:</b> Concord grape juice (480 mL/d), n=25</p> <p><b>Comparator:</b> Control, no treatment (usual intake of CGJ or red wine ≤2 times/wk), n=25</p> <p>Other interventions: polyphenol-free substitute grape-flavored drink, n=26</p> <p><u>Intervention duration:</u> 12wk</p> <p><u>Intervention compliance:</u> NR</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Intake of CGJ or red wine ≤2 times/wk (inclusion criteria)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At weeks: 0, 2, 4, 6, 8, 10, 12</li> <li>Weight measured on calibrated scales</li> <li>Body composition was measured using bioelectrical-impedance analysis</li> <li>Waist circumference was measured using a flexible tape to the nearest millimeter</li> </ul>	<p><b>Weight</b>, kg, Mean (SD)  <b>Within group:</b> Baseline, 12wk  Control: 77.6 (10.3), 77.7 (9.8), P=NS  CGJ: 79.0 (8.4), 79.7 (9.5) P=NS  <b>Between groups:</b> P=NS</p> <p><b>BMI</b>, kg/m<sup>2</sup>, Mean (SD)  <b>Within group:</b> Baseline, 12wk  Control: 27.3 (1.5), 27.1 (2.0), P=NS  CGJ: 27.0 (1.6), 27.1 (2.0), P=NS  <b>Between groups:</b> P=NS</p> <p><b>Waist circumference</b>, cm, Mean (SD)  <b>Within group:</b> Baseline, 12wk  Control: 33.4 (2.5), 33.1 (3.0), P=NS  <b>CGJ: 32.8 (2.6), 32.3 (2.8), P&lt;0.005</b>  <b>Between groups:</b> P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Energy Intake, kJ, Mean (SD)</b>  <b>Within group:</b> Baseline, 12wk  Control: 8857 (2693), 7718 (3081), P=NS  CGJ: 8865 (2865), 7868 (2649), P=NS  <b>Change over time, between groups:</b> P=NS</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: anthropometry at baseline, smoking</li> <li>Other factors considered: medications, supplements</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, physical activity</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Randomization and allocation methods NR; baseline differences in age, sex NR</li> <li>No power calculation</li> <li>Not all key confounders accounted for</li> <li>No measure of compliance</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding Source:</b>  Welch Foods Inc.</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Houchins, 2012<sup>73</sup></b>  <b>RCT, Crossover design, United States</b>  Baseline N=41, Analytic N= 34; Attrition: 17%; Power: 27 participants needed to detect a weight change difference of 1.55 kg with a SD of 2.74 (<math>\alpha = 0.05</math>, power = 0.80)</p> <p><b>Recruitment:</b> convenience sample from West Lafayette, Indiana</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): NR</li> <li>Age: 23(1); (18-38y)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI, lean grp: 20.9(0.3); BMI, ovwt/ob grp: 29.9(0.4)</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In the full sample of lean, overweight, and obese participants, there was no difference in weight change, fat change, or lean mass change between consuming solid fruits and vegetables for 8 weeks versus consuming fruit and vegetable juices for 8 weeks. There were some differences by weight status such that obese participants gained more weight after consuming beverages than solids compared to lean participants.</p>	<p><b>Intervention:</b> Beverages (commercially available to match FV of solid, with added dextrin to match fiber), n=34</p> <p><b>Comparator:</b> Solid fruits and vegetables (10% veg; 36% fresh fruit; 54% dried fruit), n=34</p> <p>Crossover design; participants randomized to beverage first-solid second (n=26) or solid first-beverage second (n=15). 1-wk baseline; 8-wk intervention; 3-wk washout; 8-wk intervention. Dietary load ~20% of individual's estimated energy requirement (Harris Benedict equation with an activity factor of 1.55). Study foods and bevs provided.</p> <p><u>Intervention duration:</u> 8wk</p> <p><u>Intervention compliance:</u> documented with ten 12-h fasted blood draws to measure plasma ascorbic acid and carotenoids</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Inclusion criteria: low fruit/vegetable consumer</li> <li>FV intake: Mean 3.1 (0.2) svg/d, including potatoes</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, end of each study arm</li> <li>Weight: measured after fasting</li> <li>Body composition: measured by air displacement plethysmography (Bod Pod), similar fasting and hydration state</li> </ul>	<p><b>Weight change</b>, kg, Mean (SD)  <u>Beverage (within intervention arm):</u>  <b>All (n=34): 1.95 (0.33), P&lt;0.0001</b>  <b>Lean (n=15): 1.61 (0.44), P=0.003</b>  <b>Overweight/obese (n=19): 2.22 (0.47), P&lt;0.0005</b>  Overweight (n=14): 1.56 (0.40)  Obese (n=5): 4.04 (1.12)  <b>Obese &gt; lean, overweight, P=0.024</b>  <u>Solid (within intervention arm):</u>  <b>All (n=34): 1.36 (0.30), P&lt;0.0001</b>  <b>Lean (n=15): 0.84 (0.53), P=0.133</b>  <b>Overweight/obese (n=19): 1.77 (0.32), P&lt;0.0005</b>  <u>Beverage vs solid</u>  All (n=34): 0.59 (2.56), P=0.19  Lean (n=15): 0.77 (2.84), P=0.31  Overweight (n=14): -0.09 (1.96), P=0.86  Obese (n=5): 1.94 (3.04), P=0.23  <b>Obese &gt; lean: P=0.02</b>  Obese vs Overweight: P=0.07</p> <p><b>Fat change</b>, kg, Mean (SD)  <u>Beverage (within intervention arm):</u>  <b>All (n=33): 1.50 (0.39), P&lt;0.0005</b>  No group effect (Data NR)  <u>Solid (within intervention arm):</u>  <b>All (n=33): 1.16 (0.33), P=0.002</b>  Lean (n=15): 0.65 (0.51)  Overweight (N=14): 1.37 (0.53)  Obese (n=5): 3.61 (0.88)  <b>Obese &gt; Lean, P=0.02</b>  <u>Beverage vs solid</u>  All (n=34): 1.13 (4.44), P=0.15  Lean (n=15): 1.95 (4.76), P=0.13  Overweight (n=14): -0.67 (2.17), P=0.27  Obese (n=5): 3.71 (6.79), P=0.29</p> <p><b>Lean mass change:</b> NS (Data NR)</p>	<p><b>TEI adjusted:</b> No</p> <p><u>El change</u>, kcal: beverage vs solid, Mean (SD)  <b>All (n=34):</b> 127 (895), P=0.41  <b>Lean (n=15):</b> 391 (894), P=0.11  <b>Overweight (n=14):</b> 6.30 (920), P=0.98  <b>Obese (n=5):</b> -327 (697), P=0.35</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: age, anthropometry at baseline</li> <li>Other factors considered: medications</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, race/ethnicity, SES, physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for; sex NR</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding Source:</b>  NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Pourahmadi, 2015<sup>77</sup></b>  <b>RCT, Iran</b>  Baseline N=80, Analytic N=75 (Attrition: 6%); Power: NR</p> <p><b>Recruitment:</b> written announcement to students at Tehran University of Medical Sciences</p> <p><b>Participant characteristics: overweight and obese females</b></p> <ul style="list-style-type: none"> <li>Total energy intake: ~1281 kcal/d</li> <li>Sex (female): 100%</li> <li>Age: (20-30y)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: Weight~72kg; BMI~28 kg/m<sup>2</sup></li> <li>Physical activity: NR; maintain usual physical activity levels</li> <li>Smoking: 100% nonsmokers (exclusion criteria current smoking)</li> </ul> <p><b>Summary of findings:</b>  In overweight and obese females, drinking tomato juice (330 mL/d) compared to water (330 mL/d) for 20 days did not change weight or BMI. There was no statistically significant difference in energy intake between the intervention and control group after 20d.</p>	<p><b>Intervention:</b> Tomato juice (330 mL/d), maintain usual diet and physical activity, n=40</p> <p><b>Comparator:</b> Water (330 L/d), maintain usual diet and physical activity, n=35</p> <p><i>Double-blind</i>  Other interventions: N/A</p> <p><u>Intervention duration:</u> 20 days</p> <p><u>Intervention compliance:</u> phone calls to participants every 3d; compliance NR</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Juice intake: intervention group asked to consume tomato juice two times a day (morning and afternoon)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 12wk follow-up</li> <li>Weight measured with light clothes and without shoes to nearest 0.1 kg using a scale</li> <li>Height measured without shoes to nearest 0.1 cm using a stadiometer</li> <li>BMI calculated as kg/m<sup>2</sup></li> </ul>	<p><b>Weight</b>, kg, t-test, Mean (SD)  <b>Change within groups:</b> Before, After  Water: 72.39 (1.19), 72.38 (1.19); P=0.64  Juice: 71.82 (1.31), 71.83 (1.32); P=0.56  <b>Change between groups:</b> P=0.75</p> <p><b>BMI</b>, kg/m<sup>2</sup>, t-test, Mean (SD)  <b>Change within groups:</b> Before, After  Water: 28.28 (0.29), 28.29 (0.29); P=0.11  Juice: 28.22 (0.35), 28.23 (0.35); P=0.482  <b>Change between groups:</b> P=0.88</p>	<p><b>TEI adjusted:</b> Yes (NS btwn groups)</p> <p><b>Energy intake</b>, kcal/d, Mean (SD)  <b>Change within groups:</b> Before, After  Water: 1228.7 (36.7), 1228.3 (36.8), P=0.11  Juice: 1332.5 (50.37), 1327.6 (50.77), P=0.05  <b>Change between groups:</b> P=0.11</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, anthropometry at baseline, smoking</li> <li>Other factors considered: total energy intake, protein, medications, supplements</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: age, race/ethnicity, SES, physical activity</li> <li>Other factors considered: timing, temporal use, sugar, fiber, energy density, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Carbohydrate, fat, and lycopene intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Power NR</li> <li>Intervention was 20 days duration</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding Source:</b>  Tabriz University of Medical Sciences</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Simao, 2013<sup>80</sup></b>  <b>NRCT, Brazil</b>  Baseline N=58, Analytic N=56 (Attrition: 3.4%); Power: NR</p> <p><b>Recruitment:</b> hospital</p> <p><b>Participant characteristics: adults with metabolic syndrome</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 76%</li> <li>Age: Mean~49y (Range: 18-60y)</li> <li>Race/ethnicity: White 70%, Non-White 30%</li> <li>SES: NR</li> <li>Anthropometrics: BMI, Mean~33 kg/m<sup>2</sup>; Waist circumference, Mean~105 cm</li> <li>Physical activity: maintain level of physical activity during intervention</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In adults with metabolic syndrome, daily intake of reduced-energy cranberry juice was not significantly associated with BMI or waist circumference after 60d.</p>	<p><b>Intervention:</b> Reduced-energy cranberry juice (0.7 L/d), n=20</p> <p><b>Comparator:</b> Control (maintain usual diet), n=36</p> <p>Other interventions: none</p> <p><u>Intervention duration:</u> 60d</p> <p><u>Intervention compliance:</u> consumption of juice: 95%</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Cranberry juice intake: NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 60d follow-up</li> <li>Weight measured to the nearest 0.1 kg using electronic scale in the morning</li> <li>Height measured to nearest 0.1 cm with a stadiometer</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>Waist circumference measured with soft tape midway between lowest rib and iliac crest</li> </ul>	<p><b>BMI</b>, kg/m<sup>2</sup>  <b>Change over time, between groups:</b>  Data NR; P=NS</p> <p><b>Waist circumference</b>, Linear regression  <b>Change over time, between groups:</b>  Data NR; P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders (no baseline differences): sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: medications</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No info on whether outcome assessors (study staff) were blinded to intervention group</li> <li>No preregistered data analysis plan</li> <li>No power calculation</li> </ul> <p><b>Funding Sources:</b>  National Council of Brazilian Research; Juxx Company</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<b>PROSPECTIVE COHORT STUDIES</b>			
<p><b>Auerbach, 2018<sup>64</sup></b>  <b>Prospective Cohort Study, Women's Health Initiative, United States</b>  Baseline N=122,970, Analytic N=49,106 (Attrition: 60.1%); Power: NR</p> <p><b>Recruitment:</b> clinical centers in 24 states</p> <p><b>Participant characteristics: postmenopausal women</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d, Mean (SD): 1636 (620)</li> <li>Sex (female): 100%</li> <li>Age: 57.9 (4.1) y</li> <li>Race/ethnicity: White 84%, African American 7.6%, Hispanic/Latino 4.0%, Asian/Pacific 3.0%</li> <li>SES: College degree or higher 48%, Annual household income ≥ \$75,000 15.4%</li> <li>Anthropometrics: Mean (SD), BMI= 26.2 (4.0) kg/m<sup>2</sup></li> <li>Physical activity: Recreational physical activity level (MET-hours/wk): 4.3 (3.9)</li> <li>Smoking: Current smoking 7.1%</li> </ul> <p><b>Summary of findings:</b>  In postmenopausal women, 100% fruit juice intake was significantly associated with increased weight over 3 years.</p>	<p><b>Exposure of interest:</b> 100% fruit juice intake (1 svg = 6 oz)</p> <p><b>Comparator:</b> 100% fruit juice intake (continuous; svg/d)</p> <p>Other exposure measures: SSB</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents usual intake</li> <li>At baseline, 3y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>100% fruit juice intake (svg/d), Mean (SD): 0.67 (0.63)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 3y follow-up</li> <li>Weight measured using standardized protocol and calibrated scales</li> </ul>	<p><b>Weight, lb/3-year change per svg/d increase</b>, Linear mixed effects model, B (95% CI):</p> <p><b>TEI unadj: 0.39 (0.10, 0.69)</b>  <b>TEI adj: 0.33 (0.04, 0.63)</b></p> <p><b>Analysis with Multiple Imputation (n=74,397)</b>  <b>TEI unadj: 0.39 (0.15, 0.63)</b>  <b>TEI adj: 0.33 (0.09, 0.58)</b></p> <p><b>Stratified by BMI group</b>  BMI 18.5-24.9 (n=20,494):  TEI unadj: 0.42 (-0.07, 0.91)  TEI adj: 0.38 (-0.11, 0.87)</p> <p>BMI 25.0-29.9 (n=18,543):  TEI unadj: 0.28 (-0.15, 0.71)  TEI adj: 0.23 (-0.20, 0.66)</p> <p>BMI 30.0-34.9 (n=9,588):  TEI unadj: 0.59 (-0.07, 1.25)  TEI adj: 0.50 (-0.15, 1.16)</p> <p>"Results did not differ in stratified analyses of 5-year increments of baseline age or baseline BMI category, and interaction terms for change in 100% fruit juice consumption and baseline age (P=.64) and baseline BMI (P=.66) were not significant" (Data NR)</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: N/A</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Hormone replacement therapy status, 3-year change in healthy eating index diet quality score</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NHLBI; NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Bes-Rastrollo, 2008<sup>9</sup></b>  <b>Prospective Cohort Study, Nurses' Health Study II, United States</b>  Baseline N=116671, Analytic N=50026 (Attrition: 57%); Power: NR</p> <p><b>Recruitment:</b> convenience sample of nurses from 14 states</p> <p><b>Participant characteristics: Women</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d, Mean (SE): 1771 (522)</li> <li>Sex (female): 100%</li> <li>Age, y, Mean (SD): 36.5 (4.6)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics, Mean (SD): BMI=24.2 (5.0) kg/m<sup>2</sup>; Weight=65.9 (14.3) kg</li> <li>Physical activity, Mean (SD): 20.4 (26.4) MET-h/wk</li> <li>Smoking: Current, 11.1%</li> </ul> <p><b>Summary of findings:</b>  Greater 8-year increase in orange juice was associated with greater 8-year weight gain in women. Eight-year change in tomato juice or apple juice intake was not significantly associated with 8-year change in weight.</p>	<p><b>Exposure of interest:</b> Tomato juice, Orange juice, Apple juice</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Tomato juice intake (categorical; tertiles) <ul style="list-style-type: none"> <li>Lowest tertile 8y change (ref)</li> <li>Highest tertile 8y change</li> </ul> </li> <li>Orange juice intake (categorical; tertiles) <ul style="list-style-type: none"> <li>Lowest tertile 8y change (ref)</li> <li>Highest tertile 8y change</li> </ul> </li> <li>Apple juice intake (categorical; tertiles) <ul style="list-style-type: none"> <li>Lowest tertile 8y change (ref)</li> <li>Highest tertile 8y change</li> </ul> </li> </ul> <p>Other exposures: skim milk, milk, low calorie cola, low calorie caffeine free cola, water, tea, decaffeinated coffee, coffee, caffeine free cola, cola, other carbonated beverages, punch</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Self-administered semi-quantitative FFQ; Represents intake during previous year</li> <li>At baseline, 8y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 8y follow-up</li> <li>Weight, self-reported through biennial questionnaires</li> </ul>	<p><b>Weight</b>, Linear regression  <b>Orange juice intake, categorical</b>  8y change in weight by 8y change in intake, between group:  <b>Lowest tertile (ref) vs Highest tertile: Data NR, P&lt;0.05</b></p> <p><b>Apple juice intake, categorical</b>  8y change in weight by 8y change in intake, between group:  Lowest tertile (ref) vs Highest tertile: Data NR, P=NS</p> <p><b>Tomato juice intake, categorical</b>  8y change in weight by 8y change in intake, between group:  Lowest tertile (ref) vs Highest tertile: Data NR, P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Postmenopausal hormone use, oral contraceptive use, changes in confounders between time periods</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposures were not well described</li> <li>Impact of missing data on analyses unclear</li> <li>Self-reported weight</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH; Spanish Ministry of Education; Fundacion Caja Madrid; Amigos de la Universidad de Navarra; AHA Established Investigator Award</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Cahill, 2012<sup>65</sup></b>  <b>Prospective Cohort Study of an 8wk weight-loss intervention, US</b>  Baseline N=67, Analytic N=58 (Attrition: 13%); Power: NR</p> <p><b>Recruitment:</b> WIC clinics, doctors' offices, and neighborhood centers</p> <p><b>Participant characteristics: overweight/obese low-income postpartum women (with infants 0-4mo)</b></p> <ul style="list-style-type: none"> <li>• Total energy intake, kcal/d: Mean (SEM)=3097.7 (175.6); Range=450.2-7112.69</li> <li>• Sex (female): 100%</li> <li>• Age, y: Mean (SD)=28.0 (0.7); Range=19-39</li> <li>• Race/ethnicity: Hispanic 53%, White 35%, African American 12%</li> <li>• SES: Education: ≤High school 14%, Partial college 43%, ≥College graduate 26%; Living with spouse/partner 83%</li> <li>• Anthropometrics, Mean (SD): Weight, 84.8 (2.4) kg; Body fat %, 41.3 (0.8); Waist circumference, 99.7 (2.0) cm; BMI, 32.0 (0.8) kg/m<sup>2</sup></li> <li>• Physical activity: Aerobic exercise, Mean (SEM)=1.1 (0.4) hr/wk</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In low-income postpartum women, fruit juice intake was not significantly associated with postpartum weight change.</p>	<p><b>Intervention:</b> Fruit juice intake (not clear if its 100% fruit juice)</p> <p><b>Comparator:</b> Fruit juice intake (continuous; svg/d)</p> <p>Other exposures: none</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated FFQ; represents usual intake</li> <li>• At baseline, 10wk follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Fruit juice (svg/d): Mean (SEM)=0.8 (0.1); Range=0.0-4.25</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 10wk follow-up</li> <li>• Weight measured to nearest 0.1 kg via electronic scale on one occasion without shoes in light clothing</li> <li>• Height measured to nearest 0.1 cm using wall-mounted stadiometer</li> <li>• Body fat percentage measured via electronic scale on one occasion without shoes in light clothing</li> </ul>	<p><b>Weight</b>, kg, Linear regression  <b>Change per svg/d increase:</b>  B: -0.247, P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, anthropometry at baseline</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, race/ethnicity, SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  <b>gestational weight gain</b></p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Exposure not clearly defined</li> <li>• Outcome is specific to postpartum weight loss (may not be generalizable to non-postpartum women)</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Texas Department of Health Minority Education Grant, TX Coordination Board</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b><u>Drapeau, 2004</u></b><sup>16</sup></p> <p><b>Prospective Cohort Study, Quebec Family Study, Canada</b></p> <p>Baseline N=NR, Analytic N=248 (Attrition: NR); Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 54.9%</li> <li>• Age: Mean=39.6 y, SEM=0.9, Range: 18-65</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI, Mean=25.3, SEM=0.3, Range: 17.4-55.6</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>Change in fruit juice intake not associated with change in weight and adiposity measures over 6 years in adults.</p>	<p><b>Exposure of interest:</b> Fruit juice (non-sweetened fruit juice: orange, apple, pineapple)</p> <p><b>Comparator:</b> Fruit juice intake (continuous; units NR)</p> <p>Other exposures: low-fat milk, regular milk, fruit juice, fruit beverage, regular sodas</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Three-day dietary record (2 weekdays, 1 weekend day); Represents usual intake</li> <li>• At baseline, 6y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• Weight measured by study personnel</li> <li>• Body fat percentage estimated using underwater weighing technique and the Siri formula</li> <li>• Waist circumference measured by study personnel using Airlie Conference procedures</li> <li>• Sum of 6 skinfold thicknesses (triceps, biceps, medial calf, subscapular, suprailiac, and abdominal) measured by study personnel</li> </ul>	<p><b>Fruit juice intake, continuous</b></p> <p>6y change by 6y change in intake, linear regression</p> <p><b>Weight:</b> NS, Data NR</p> <p><b>Body fat percentage:</b> NS, Data NR</p> <p><b>Waist circumference:</b> NS, Data NR</p> <p><b>Sum of 6 skinfold thicknesses:</b> NS, Data NR</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, anthropometry at baseline, physical activity</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, race/ethnicity, SES, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Did not account for all key confounders</li> <li>• Validation of 3-day dietary record unclear</li> <li>• No information on missing data</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b></p> <p>Canadian Institutes of Health Research</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Duffey, 2010<sup>18</sup></b>  <b>Prospective Cohort Study, Coronary Artery Risk Development in Young Adults (CARDIA), United States</b>  Baseline N=5115, Analytic N=2444 (Attrition: 52%); Power: NR</p> <p><b>Recruitment:</b> convenience sample through phone and door-to-door recruitment</p> <p><b>Participant characteristics: young adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR; energy from food, Mean: 2347 kcal</li> <li>Sex (female): 53.5%</li> <li>Age, Mean (SD): 25.0 y (3.6)</li> <li>Race/ethnicity: Black 47.4%</li> <li>SES: NR</li> <li>Anthropometrics, Mean (SD): BMI, 24.5 (5.0); WC, 77.3 cm (10.9)</li> <li>Physical activity, Mean (SD): 429 exercise units/wk (302)</li> <li>Smoking: Current 28.1%, Former 13.1%, Never 58.7%</li> </ul> <p><b>Summary of findings:</b>  Fruit juice intake was not associated with incidence of high waist circumference (WC) at 20y follow-up.</p>	<p><b>Exposure of interest:</b> Fruit juice (does not include sweetened 'fruit drinks')</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Fruit juice intake (continuous; kcal/d)</li> <li>Fruit juice intake (categorical; quartiles)</li> </ul> <p>Other exposures: low-fat milk, whole-fat milk, SSBs</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Semi-quantitative, interviewer-administered, validated diet history food-frequency questionnaire; Represents previous month</li> <li>At baseline, 7y follow-up (averaged)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Fruit juice: 95% consuming <ul style="list-style-type: none"> <li>Among consumers: Mean=121 kcal/d, SE=2</li> </ul> </li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At 20y follow-up</li> <li>WC at minimum abdominal girth measured in duplicate; High WC defined as WC&gt;88cm (women) or &gt;102cm (men)</li> </ul>	<p><b>High WC</b>, Poisson regression, RR (95% CI)</p> <p><b>Fruit juice intake, categorical</b>  1.00 (0.92, 1.09), P for trend = 0.999</p> <p><b>Fruit juice intake, continuous</b>  0.98 (0.90, 1.06)</p>	<p><b>TEI adjusted:</b> Yes (energy from food and other beverages)</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake (energy from food and other beverages), alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  CARDIA exam center</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Did not account for all key confounders</li> <li>Validity of 3-day diet record unclear</li> <li>Impact of missing data on analyses unclear</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Danone Research Center; NIH; UNC-CH Center for Environmental Health and Susceptibility; UNC-CH Clinic Nutrition Research Center; Carolina Population Center</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Ferreira-Pêgo, 2016<sup>68</sup></b>  <b>Prospective analyses of RCT, PREDIMED (PREvención con Dieta MEDiterránea), Spain</b>  Baseline N= 2094; Analytic N=1,868; Attrition: 11%; Power: NR</p> <p><b>Recruitment:</b> participants were selected from all of the PREDIMED recruitment centers with biochemical determinations available for a follow-up of ≥2 y; all participants were at high risk of CVD due to the presence of T2D or ≥3 risk factors: current smoking, hypertension, high LDL cholesterol, low HDL cholesterol, overweight or obese, or family history of premature CVD but did not have MetSyn</p> <p><b>Participant characteristics: adults, high risk for CVD</b></p> <ul style="list-style-type: none"> <li>• Total energy intake, kcal/d, Mean (SD): 2322.6 (~530)</li> <li>• Sex (female): 52.5%</li> <li>• Age: ~67y (~6y)</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI: 28.3 (~3.5)</li> <li>• Physical activity: Leisure time MET-min/d: ~274 (252)</li> <li>• Smoking: ~58%: Never; ~17% Current; ~26% Former</li> </ul> <p><b>Summary of findings:</b>  In a sample of older adults at high-risk for CVD, the highest level of natural fruit juice consumption (&gt;5 serv/wk) was associated with greater risk of abdominal obesity over a follow-up period of ≥2y.</p>	<p><b>Exposure of interest:</b></p> <ul style="list-style-type: none"> <li>• Fruit juice (natural fruit juices: freshly extracted juice, for which the only procedure accepted was the squeezing of the whole piece of fruit); 1svg=200mL</li> </ul> <p><b>Comparators:</b> Fruit juice, categorical</p> <ul style="list-style-type: none"> <li>• &lt;1 svg/wk (Ref)</li> <li>• 1-5 svg/wk</li> <li>• &gt;5 svg/wk</li> </ul> <p>Other exposures measured: SSBs, LNCSBs</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated FFQ assessing habitual intake for previous year</li> <li>• At baseline, annually</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• During follow up: Mean 29.3 mL/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• Baseline, yearly during follow-up period of ≥2y</li> <li>• Weight: measured by trained personnel with calibrated scales</li> <li>• Height: measured by trained personnel with a wall-mounted stadiometer.</li> <li>• Waist circumference measured using an anthropometric tape midway between the lower rib and the superior border of the iliac crest</li> <li>• Abdominal obesity: waist circumference ≥88cm in women and ≥102 cm in men</li> </ul>	<p><b>Abdominal obesity.</b> Multivariable time-dependent Cox proportional regression, HR (95% CI)  <b>Natural fruit juices:</b>  &lt;1 serv/wk: Ref  1-5 serv/wk: 0.97 (0.76, 1.24)  <b>&gt;5 serv/wk: 1.52 (1.02, 2.25)</b>  P for trend: 0.08</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, alcohol (overall alcohol intake &amp; alcohol squared in grams per day)</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Intervention group, average consumption during the follow-up of dietary variables as continuous variables, prevalence of MetSyn components at baseline</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No information on whether or not amount of missing data varied across exposure groups</li> <li>• Follow-up time differs among participants</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Spanish Ministry of Health, the Thematic Network, FEDER (European Regional Development Fund), the Centre Català de la Nutrició de l'Institut d'Estudis Catalans, and the Fundació "LaMarat" o de TV3"</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Fresan, 2016<sup>22</sup></b>  <b>Prospective Cohort Study, SUN Cohort, Spain</b>  Baseline N=17984, Analytic N=15765 (Attrition: 12%); Power: NR</p> <p><b>Recruitment:</b> Convenience sample of university graduates</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~2342 kcal/d</li> <li>Sex (female): 59.8%</li> <li>Age, Mean (SD): 37.9 (11.7) y</li> <li>Race/ethnicity: NR</li> <li>SES: University graduate 100%</li> <li>Anthropometrics, Mean (SD): BMI, 23.49 (3.5) kg/m<sup>2</sup></li> <li>Physical activity: Mean~21.7 MET-h/wk</li> <li>Smoking: Current smoker 21.6%, Former smoker 28.4%</li> </ul> <p><b>Summary of findings:</b>  Replacement of fresh orange or non-orange juice or bottled juice with water was not significantly associated with incidence of obesity or 4y weight change.</p>	<p><b>Exposure of interest:</b> Fresh orange juice, Fresh non-orange juice, Bottled juice (1svg = 200mL)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Substituting water for fresh orange juice (continuous; svg/d water increase/svg/d decrease fresh orange juice)</li> <li>Substituting water for fresh non-orange juice (continuous; svg/d water increase/svg/d decrease fresh non-orange juice)</li> <li>Substituting water for bottled juice (continuous; svg/d water increase/svg/d bottled juice)</li> </ul> <p>Other exposures: Skim milk, reduced-fat milk, whole milk, milk shakes, SSSBs, diet soda beverages, regular coffee, decaffeinated coffee, water</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Semi-quantitative FFQ previously validated in Spain; Represents intake during previous year</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Juices: Mean~3.1 svg/wk</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, every 2y</li> <li>BMI from self-reported weight and height</li> <li>Obesity defined as BMI ≥30 kg/m<sup>2</sup></li> </ul>	<p><b>Obesity</b>, OR (95% CI), logistic regression  <b>Substitution of 1 svg/d water for 1 svg/d orange juice, continuous</b>  1.06 (0.90, 1.24)</p> <p><b>Substitution of 1 svg/d water for 1 svg/d fresh non-orange juice, continuous</b>  1.06 (0.73, 1.52)</p> <p><b>Substitution of 1 svg/d water for 1 svg/d bottled juice, continuous</b>  0.86 (0.73, 1.02)</p> <p><b>4y Weight change</b>, g, Mean (95% CI), linear regression  <b>Substitution of 1 svg/d water for 1 svg/d orange juice, continuous</b>  7 (-189, 202)</p> <p><b>Substitution of 1 svg/d water for 1 svg/d fresh non-orange juice, continuous</b>  -342 (-760, 76)</p> <p><b>Substitution of 1 svg/d water for 1 svg/d bottled juice, continuous</b>  -137 (-400, 127)</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Personal history of obesity, family history of obesity, following a special diet, adherence to Mediterranean dietary pattern, snacking between meals, weight change in past 5y</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Selection into study may have been related to exposure and outcome</li> <li>Exposure data only measured at baseline</li> <li>Weight self-reported</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Spanish Ministry of Health; Navarra Regional Government; University of Navarra</p>

**Funtikova, 2015<sup>23</sup>**

**Prospective Cohort Study, Spain**

Baseline N=3058, Analytic N=2112  
(Attrition: 31%); Power: NR

**Recruitment:** Randomly selected  
population-based sample

**Participant characteristics: adults**

- Total energy intake, Mean: ~11.2 MJ/d kcal/d
- Sex (female): 52.6%
- Age, Mean: ~49.2y
- Race/ethnicity: NR
- SES: Higher education ~37%
- Anthropometrics, Mean: WC, ~89.6 cm
- Physical activity, Mean: ~200 MET-min/d (leisure time)
- Smoking: Current smoker ~26%

**Summary of findings:**

In adults, juice intake was not significantly associated with waist circumference (WC) or odds of developing abdominal obesity.

**Exposure of interest:** Juices (100% juices including commercial and natural fruit/vegetable juices – apple, peach, orange, grape, and tomato)  
(1 svg = 200mL)

**Comparators:**

- Juice intake (continuous; 100 kcal/d)
- Juice intake (categorical; svg/d)
  - No consumption (ref)
  - <1
  - ≥1
- Juice intake (categorical; change in consumption)
  - No consumption (ref)
  - Decrease
  - Increase
  - Maintain

Other exposures: whole milk, skim and low-fat milk, soft drinks

**Exposure assessment method and timing:**

- Validated, 166-item FFQ administered by trained interviewer; Represents intake during previous year
- At baseline, 9y follow-up

**Study beverage intake:**

- Juices, mL/d, mean (SD): 64 (114)

**Outcome assessment methods/timing:**

- At baseline, 9y follow-up
- WC measured midway between lowest rib and iliac crest with participant lying horizontally
- Abdominal obesity defined as >102 cm for men and >88 cm for women

**Abdominal obesity**, OR (95% CI), logistic regression

**Juices, categorical**

Incidence by baseline intake:

No consumption (ref)

<1 svg/d: 0.98 (0.72, 1.31)

≥1 svg/d: 0.74 (0.49, 1.13)

**Men (n=756)**

No consumption (ref)

<1 svg/d: 1.15 (0.72, 1.82)

≥1 svg/d: 1.23 (0.64, 2.36)

P trend =0.62

**Women (n=723)**

No consumption (ref)

<1 svg/d: 0.87 (0.60, 1.30)

≥1 svg/d: 0.53 (0.35, 1.00)

**P trend = 0.027**

**WC**, cm, Mean (95% CI), linear regression

**Juices, continuous**

Change per 100 kcal/d increase:

-0.03 (-0.74, 0.68), P=0.93

**Men:** -0.25 (-1.26, 0.76), P=0.63

**Women:** 0.06 (-0.95, 1.07), P=0.91

**WC**, cm, Change by change in consumption,

**Juices (change in consumption), categorical**

Mean (95% CI), linear regression:

No consumption (ref)

Decrease: 0.25 (-0.67, 1.17), P=0.59

Increase: 0.25 (-0.73, 1.22), P=0.62

Maintain: 0.15 (-1.93, 2.24), P=0.89

**Men (n=1000)**

No consumption (ref)

Decrease: 0.50 (-0.71, 1.72), P=0.42

Increase: -0.81 (-2.10, 0.48), P=0.22

Maintain: 0.30 (-2.05, 2.56), P=0.60

**Women (n=1112)**

No consumption (ref)

Decrease: 0.10 (-1.35, 1.56), P=0.69

Increase: 1.05 (-0.40, 2.51), P=0.16

Maintain: 0.38 (-1.80, 2.55), P=0.74

**TEI adjusted:** Yes

**Confounders accounted for:**

- Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking
- Other factors considered: total energy intake

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:** Modified Mediterranean diet score, energy under- and over-reporting, dieting (change in consumption models only), other beverage intake

**Limitations:**

- Not all key confounders accounted for
- Attrition 31% without information on non-completers
- No preregistered analysis plan

**Funding sources:**

Catalan Government; Carlos III Health Institute European Fund for Regional Development; Catalonian Agency for the Administration of University and Research Grants

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Halkjaer, 2009</b><sup>71</sup></p> <p><b>Prospective Cohort Study; Danish Diet, Cancer, and Health study; Denmark</b> Baseline N= 57053, Analytic N= 42696; Attrition: 25%; Power: NR</p> <p><b>Recruitment:</b> identified from the computerized records of the Civil Registration System in Denmark</p> <p><b>Participant characteristics: middle-aged adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 53%</li> <li>• Age: ~56y (50-64y)</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI ~25 kg/m<sup>2</sup></li> <li>• Physical activity: ~55% perform ≥30min sport/wk</li> <li>• Smoking: ~33% current smokers</li> </ul> <p><b>Summary of findings:</b> There was no significant association between juice intake and change in WC over 5 years in middle-aged adults.</p>	<p><b>Exposure of interest:</b> Juices (vegetable and fruit juice; <i>not clear if 100% juice</i>)</p> <p><b>Comparators:</b> Juice (continuous; per 60 kcal/d)</p> <p>Other exposure measures: soft drinks, coffee, tea</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated FFQ; represents usual intake</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Juice: Median~3.7 kcal/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 5y follow-up</li> <li>• Height, weight, waist circumference, hip circumference measured at baseline</li> <li>• <i>Follow-up weight and WC were self-report</i></li> <li>• Waist circumference measured at the smallest horizontal circumference between the ribs and iliac crest (the natural waist), or, in case of an indeterminable waist narrowing, halfway between the lower rib and the iliac crest; SELF-REPORTED: measuring tape was provided, participants were told to measure WC at the level of the umbilicus</li> <li>• Hip circumference was measured at the largest horizontal expansion of the buttocks</li> <li>• BMI calculated</li> </ul>	<p><b>WC</b>, cm, 5yr change per 60 kcal/d_ juice, Linear regression, <math>\beta</math> (95% CI) <b>Women:</b> -0.15 (-0.38, 0.09) <b>Men:</b> 0.11 (-0.09, 0.31) Interaction, P=0.09</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Attrition 25% without information on non-completers</li> <li>• Exposure data only measured at baseline</li> <li>• WC self-reported</li> <li>• No preregistered data analysis plan; no reporting of other outcomes measured (weight, BMI, hip circumference)</li> </ul> <p><b>Funding sources:</b> National Danish Research Foundation; Diet, Obesity and Genes project, supported by European Community</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Mozaffarian, 2011</b><sup>42</sup></p> <p><b>Prospective Cohort Study, Nurses Health Study (NHS) + NHS II + Health Professionals Follow-Up Study (HPS), United States</b></p> <p>NHS: Analytic N=50,422 (Attrition: NR); Power: NR NHS II: Analytic N=47,898 (Attrition: NR) Power: NR HPS: Analytic N=22,557 (Attrition: NR); Power: NR</p> <p><b>Recruitment:</b> professional organizations or from occupation mailing house lists</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): NHS and NHS II 100%, HPS 0%</li> <li>• Age, y, Mean (SD): NHS 52.2 (7.2), NHS II 37.5 (4.1), HPS 50.8 (7.5)</li> <li>• Race/ethnicity: primarily white</li> <li>• SES: primarily educated</li> <li>• Anthropometrics, Mean (SD): BMI (kg/m<sup>2</sup>), NHS 23.7 (1.4), NHS II 23.0 (2.7), HPS 24.7 (1.1)</li> <li>• Physical activity, MET-hr/wk, Mean (SD): NHS 14.8 (9.9), NHS II 21.6 (25.9), HPS 22.9 (15.1)</li> <li>• Smoking: Never smoker 53%, Past smoker 33%, Current smoker 13%, Missing 1%</li> </ul> <p><b>Summary of findings:</b></p> <p>In adults, greater fruit juice intake was significantly associated with increased weight gain.</p>	<p><b>Exposure of interest:</b> 100% fruit juice intake (apple juice or cider, orange, grapefruit, and other fruit juice)</p> <p><b>Comparator:</b> Fruit juice intake (continuous; svg/d)</p> <p>Other exposure measures: milk, SSBs, diet soda</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated questionnaire; represents usual dietary intake</li> <li>• At baseline, every 4y over 12- to 20-y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Fruit juice intake, svg/d, Mean (SD): NHS 0.8 (0.4), NHS II 0.6 (0.7), HPS 0.8 (0.4)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, and every 2y over 12- to 20-y follow-up</li> <li>• Weight was collected via self-report from questionnaire</li> </ul>	<p><b>Weight</b>, lb, Linear regression, <math>\beta</math> (95% CI)</p> <p><b>Change per svg/d increase:</b>  <b>NHS: 0.26 (0.20, 0.32), P&lt;0.001</b>  <b>NHS II: 0.49 (0.41, 0.58), P&lt;0.001</b>  <b>HPS: 0.17 (0.10, 0.25), P&lt;0.001</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Television watching, sleep duration, dietary variables (fruits, vegetables, whole-fat and low-fat dairy, potato chips, potatoes/fries, whole grains, refined grains, sweets and desserts, processed and unprocessed meats, trans fat, fried foods at and away from home)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Weight was self-reported</li> </ul> <p><b>Funding sources:</b>  NIH; Searle Scholars Program</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Odegaard, 2010<sup>76</sup></b>  <b>Prospective Cohort Study, Singapore Chinese Health Study, Singapore</b>  Baseline N=51813, Analytic N=43580 (Attrition: 16%); Power: NR</p> <p><b>Recruitment:</b> Convenience sample recruited through mail invitation</p> <p><b>Participant characteristics:</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d, Mean: ~1600</li> <li>Sex (female): ~48%</li> <li>Age: 54.8 (7.5) (Range 45-74y)</li> <li>Race/ethnicity: 100% Chinese</li> <li>SES: Education: Secondary: ~33%</li> <li>Anthropometrics: BMI: ~23 kg/m<sup>2</sup></li> <li>Physical activity: Moderate activity: ~50 min/wk</li> <li>Smoking, ever: ~26%</li> </ul> <p>Note: characteristics are broken down by beverage consumption amount in paper</p> <p><b>Summary of findings:</b>  In a sample of Chinese adults living in Singapore, intake of fruit and vegetable juice was not related to change in weight over an average of 5.7 years</p>	<p><b>Exposure of interest:</b> Fruit and vegetable juices (1 glass = 237mL or ~1cup); unclear if 100% juice</p> <p><b>Comparators:</b> Juice intake (categorical)</p> <ul style="list-style-type: none"> <li>Never or hardly ever (0 serv, Ref)</li> <li>Monthly (1-3 serv/mo)</li> <li>1 serv/wk</li> <li>≥2 serv/wk</li> </ul> <p>Other exposures measured: SSBs</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents usual intake over the past year</li> <li>At baseline only</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Never or hardly ever (0 serv): 82.0%</li> <li>Monthly (1-3 serv/mo): 10.1%</li> <li>1 svg/wk: 4.1%</li> <li>≥2 svg/wk: 3.8%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>Baseline and follow up (avg=5.7y later)</li> <li>Weight &amp; height: self-reported</li> <li>BMI calculated as kg/m<sup>2</sup></li> </ul>	<p><b>Change in weight</b>, kg, Linear Regression</p> <p><b>Juice intake:</b>  NS; Data NR</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, (race/ethnicity), SES, anthropometry at baseline, smoking</li> <li>Other factors considered: alcohol, fiber</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b> Dialect, year of interview, person-years, total intake (g/d) or fruits, vegetables, dairy, meat, candy, desserts, saturated fat, juice, coffee</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure assessed at baseline only</li> <li>Categories of beverage intake measured vary from those used in analyses</li> <li>Majority of participants consumed no juice</li> <li>Self-reported height and weight data</li> <li>Participants who died between assessments were excluded from these analyses</li> <li>Missing data may have differentially affected exposure groups</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Pan, 2013<sup>46</sup></b>  <b>Prospective Cohort Study, Nurses Health Study (NHS) + NHS II + Health Professionals Follow-Up Study (HPS), United States</b>  <i>NHS</i>: Analytic N=50,013 (Attrition: NR); Power: NR  <i>NHS II</i>: Analytic N=52,987 (Attrition: NR); Power: NR  <i>HPS</i>: Analytic N=21,988 (Attrition: NR); Power: NR</p> <p><b>Recruitment:</b> professional organizations or from occupation mailing house lists</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 82%</li> <li>Age: Mean~47y</li> <li>Race/ethnicity: primarily white</li> <li>SES: primarily educated</li> <li>Anthropometrics: Overweight 31%, Obesity 17%, BMI: Mean~25 kg/m<sup>2</sup></li> <li>Physical activity: Mean~18 MET-hr/wk</li> <li>Smoking: Never smoker 54%, Past smoker 33%, Current smoker 13%</li> </ul> <p><b>Summary of findings:</b>  In adults, when stratified by age or baseline BMI, greater fruit juice intake was significantly associated with increased weight gain.</p>	<p><b>Exposure of interest:</b> Fruit juice intake (apple, orange, grapefruit, and other juice)</p> <p><b>Comparator:</b> Fruit juice intake (continuous; svg/d)</p> <p>Other exposure measures: milk, water, SSBs, diet beverages, coffee, tea</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents usual intake of foods and beverages</li> <li>At baseline, every 4y over 16- to 20-y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Fruit juice intake, svg/d, Mean (5<sup>th</sup>-95<sup>th</sup>%): NHS 0.83 (0-2.29), NHS II 0.62 (0-2.0), HPS 0.78 (0-2.43)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, and every 2y over 16- to 20-y follow-up</li> <li>Weight was collected via self-report from questionnaire</li> </ul>	<p><b>Weight</b>, kg, Linear regression, <math>\beta</math> (95% CI)  <b>Change per svg/d increase:</b>  NHS: 0.24 (0.20, 0.28), P=NR  NHS II: 0.26 (0.22, 0.30), P=NR  HPS: 0.15 (0.10, 0.19), P=NR  <b>Stratified by age:</b> <math>\leq 50y</math>, <math>&gt;50y</math>  NHS: 0.23 (0.15, 0.31), 0.42 (0.38, 0.46), P=0.24  <b>NHS II: 0.28 (0.24, 0.32), 0.19 (0.09, 0.29), P=0.04</b>  HPS: 0.15 (0.07, 0.23), 0.15 (0.09, 0.20), P=0.76  <b>Stratified by BMI (kg/m<sup>2</sup>):</b> <math>&lt;25</math>, 25-29.9, <math>\geq 30</math>  <b>NHS: 0.07 (0.03, 0.10), 0.26 (0.19, 0.32), 0.60 (0.47, 0.74), P&lt;0.001</b>  <b>NHS II: 0.13 (0.09, 0.16), 0.33 (0.25, 0.41), 0.55 (0.42, 0.68), P&lt;0.001</b>  <b>HPS: 0.06 (0.01, 0.11), 0.16 (0.10, 0.23), 0.55 (0.32, 0.79), P&lt;0.001</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: sugar, protein, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: total energy intake, timing, temporal use, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Television watching, dietary variables (fruits, vegetables, whole grain, refined grain, potatoes, potato chips, red meat, other dairy products, sweets and deserts, nuts, fried foods, and trans fat), other beverage variables</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Weight was self-reported</li> </ul> <p><b>Funding sources:</b>  NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Rautiainen, 2015<sup>78</sup></b>  <b>Prospective Cohort Study, Women's Health Study (RCT), United States</b>  Baseline N=39876, Analytic N=18146  (Attrition: 54%); Power: NR</p> <p><b>Recruitment:</b> female health professionals contacted via mail</p> <p><b>Participant characteristics: normal BMI, ≥45yo women</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~1710 kcal/d</li> <li>Sex (female): 100%</li> <li>Age: ≥45y, Mean~53y</li> <li>Race/ethnicity: "predominantly Caucasian"</li> <li>SES: "predominantly health care professionals"</li> <li>Anthropometrics: BMI 18.5-&lt;25 kg/m<sup>2</sup></li> <li>Physical activity: Mean~17 MET hrs</li> <li>Smoking: 14.5% current smokers</li> </ul> <p><b>Summary of findings:</b>  In women 45 years and older, when controlling for energy intake, fruit juice intake was significantly associated with lower risk of becoming overweight or obese at 16y follow-up.</p>	<p><b>Exposure of interest:</b> Fruit juice (grapefruit, orange, apple, and other juice; does not specifically say '100%')</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Fruit juice intake (categorical; svg/d): <ul style="list-style-type: none"> <li>Quintile 1: &lt;0.1 (ref)</li> <li>Quintile 2: 0.1 to &lt;0.3</li> <li>Quintile 3: 0.3 to &lt;0.5</li> <li>Quintile 4: 0.5 to &lt;0.8</li> <li>Quintile 5: ≥0.8</li> </ul> </li> </ul> <p>Other exposure measures: N/A</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated semi-quantitative FFQ; represents usual intake during previous year</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Fruit juice intake (svg/d): &lt;0.1, 23%; 0.1 to &lt;0.3, 18%; 0.3 to &lt;0.5, 20%; 0.5 to &lt;0.8, 20%; ≥0.8, 19%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, and 2, 3, 5, 6, 9y follow-up during RCT, then annually from 11-17y during observational follow-up (Mean follow-up: 15.9y)</li> <li>Weight (lb) and height (inches) were self-reported</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>Overweight: BMI 25 to &lt;30 kg/m<sup>2</sup></li> <li>Obese: BMI ≥30 kg/m<sup>2</sup></li> </ul>	<p><b><u>Incident overweight/Obesity (BMI ≥25 kg/m<sup>2</sup>)</u></b>, among normal BMI at baseline, Cox proportional hazard, HR (95% CI)  Q1 (n=4130): ref  Q2 (n=3287): 0.98 (0.91, 1.04)  <b>Q3 (n=3615): 0.79 (0.73, 0.84)</b>  <b>Q4 (n=3573): 0.88 (0.82, 0.95)</b>  <b>Q5 (n=3518): 0.81 (0.76, 0.88)</b>  <b>P-trend &lt;0.0001</b></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, supplements, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications</li> </ul> <p><b>Additional model adjustments:</b>  Randomization treatment assignment, history of hypercholesterolemia or hypertension, postmenopausal status, postmenopausal hormone use</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure not clearly defined</li> <li>Exposure data only measured at baseline</li> <li>Attrition 54% without information on non-completers</li> <li>Weight and height self-reported</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH; Swedish Council of Working Life and Social Research</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Limitations
<p><b>Romaguera, 2011<sup>49</sup></b>  <b>Prospective Cohort Study, European Prospective Investigation into Cancer and Nutrition (EPIC); Italy, UK, Netherlands, Germany, Denmark</b>  Baseline N=102346 Analytic N=48631 (Attrition: 52.5%); Power: NR</p> <p><b>Recruitment:</b> invited general population via mail or in person</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 59.5%</li> <li>• Age: 20-60y</li> <li>• Race/ethnicity: Italy 10.4%, UK 12.9%, Netherlands 13.3%, Germany 17.8%, Denmark 45.5%</li> <li>• SES: NR</li> <li>• Anthropometrics: NR</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In men and women, juice intake was not significantly associated with WC for a given BMI at 5.5y follow-up.</p>	<p><b>Exposure of interest:</b> Juice intake</p> <p><b>Comparator:</b> Juice intake (continuous; 100 kcal/d)</p> <p>Other exposure measures: milk, soft drinks, coffee, tea, and non-alcoholic beverages</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Country-specific validated FFQ; represents usual food intakes</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Juice intake, g/d, Mean (SD): Men, 63.76 (117.91), Range=31.19-189.97; Women, 76.50 (128.63), Range=35.24-119.77</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 5.5y follow-up</li> <li>• Weight and height measured using standard protocol or via self-report</li> <li>• Waist circumference (WC) measured either midway between the lowest rib and iliac crest, at the narrowest torso circumference, or via self-report</li> <li>• BMI calculated as weight (kg) divided by height (m) squared</li> <li>• Waist circumference for a given body mass index (<math>WC_{BMI}</math>) calculated as the residual values from gender- and centre-specific regression equations of WC on BMI using baseline and follow-up values of WC and BMI</li> </ul>	<p><math>\Delta WC_{BMI}</math>, cm/y; Association between intake and annual change in WC for given BMI; <math>\beta^2</math> (95% CI), Linear regression</p> <p><b>All:</b> -0.01 (-0.03, 0.00), P=0.100  <b>Men:</b> -0.01 (-0.02, 0.01), P=0.315  <b>Women:</b> -0.02 (-0.05, 0.01), P=0.211  <i>Interaction by gender:</i> P=NS</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: N/A</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Follow-up duration, menopausal status and hormone replacement therapy use (in women)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Methods of outcome assessment differed among participants; some data was self-reported</li> <li>• Exposure data only measured at baseline</li> <li>• No information on non-completers</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  European Union; Danish Strategic Research Council</p>

**Table 11. Risk of bias for randomized controlled trials examining 100% juice consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>xxiii, xxiv</sup>**

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Aptekmann, 2010 <sup>63</sup>	Some Concerns	Low	Low	Low	Some Concerns
Hollis, 2009 <sup>72</sup>	High	Some Concerns	Low	Low	Some Concerns
Houchins, 2012 <sup>73</sup>	Low	Low	Low	Low	Some Concerns
Pourahmadi, 2015 <sup>77</sup>	Low	Low	Low	Low	Some Concerns

<sup>xxiii</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xxiv</sup> Possible ratings of low, some concerns, or high determined using the "[Cochrane Risk-of-bias 2.0](#)" (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). *Cochrane Methods. Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). [dx.doi.org/10.1002/14651858.CD201601](https://doi.org/10.1002/14651858.CD201601).)

**Table 12. Risk of bias for the non-randomized controlled trial examining 100% juice consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>xxv, xxvi</sup>**

	Confounding	Selection of participants	Classification of interventions	Deviations from intended interventions	Missing data	Outcome measurement	Selection of the reported result
Simao, 2013 <sup>80</sup>	Serious	Low	Low	Low	Low	Moderate	Moderate

<sup>xxv</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xxvi</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the “[Risk of Bias in Non-randomized Studies of Interventions \(ROBINS-I\) tool](#)” (Sterne JAC, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JPT. ROBINS-I: a tool for assessing risk of bias in non-randomized studies of interventions. *BMJ* 2016; 355; i4919; doi: 10.1136/bmj.i4919.)

**Table 13: Risk of bias for prospective cohort studies examining 100% juice consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>xxvii, xxviii</sup>**

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Auerbach, 2018 <sup>64</sup>	Moderate	Low	Low	Low	Low	Low	Moderate
Bes-Rastrollo, 2008 <sup>9</sup>	Serious	Low	Moderate	Low	Moderate	Moderate	Moderate
Cahill, 2012 <sup>65</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Drapeau, 2004 <sup>16</sup>	Serious	Low	Moderate	Low	Serious	Low	Moderate
Duffey, 2010 <sup>18</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Ferreira-Pego, 2016 <sup>68</sup>	Serious	Moderate	Low	Moderate	Low	Low	Moderate
Fresan, 2016 <sup>22</sup>	Serious	Moderate	Low	Low	Low	Moderate	Moderate
Funtikova, 2015 <sup>23</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Halkjaer, 2009 <sup>71</sup>	Serious	Low	Moderate	Low	Moderate	Serious	Serious
Mozaffarian, 2011 <sup>42</sup>	Serious	Moderate	Low	Low	Low	Serious	Moderate
Odegaard, 2010 <sup>76</sup>	Serious	Low	Moderate	Moderate	Moderate	Serious	Moderate
Pan, 2013 <sup>46</sup>	Serious	Moderate	Low	Low	Low	Serious	Moderate
Rautiainen, 2015 <sup>78</sup>	Serious	Low	Moderate	Moderate	Moderate	Serious	Moderate
Romaguera, 2011 <sup>49</sup>	Moderate	Low	Low	Low	Moderate	Moderate	Moderate

<sup>xxvii</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xxviii</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

## BEVERAGE: SUGAR-SWEETENED BEVERAGES (SSB)

What is the relationship between beverage consumption (sugar-sweetened beverages) and growth, size, body composition and risk of overweight and obesity?

### Conclusion statements and grades

Moderate evidence suggests that higher sugar-sweetened beverage intake is associated with greater adiposity in children. (Grade: Moderate)

Limited evidence suggests that higher sugar-sweetened beverage intake is associated with greater adiposity in adults. (Grade: Limited)

Insufficient evidence is available to determine the relationship between sugar-sweetened beverages compared with low- and no- calorie sweetened beverages on adiposity in children. (Grade: Grade not assignable)

Limited evidence suggests no association between sugar-sweetened beverages compared with low- and no- calorie sweetened beverages on adiposity in adults. (Grade: Limited)

### Summary of the evidence

- 76 studies were identified through a literature search from June 2012 to June 2019 were included in this systematic review.<sup>1,2,15,17,22,23,27,31,41,46,59,61,62,64,66,68,70,83-141</sup> Studies were synthesized based on comparator (no/different amount of sugar-sweetened beverage or low/no-calorie sweetened beverage) and age of participants (children or adults).
  - Sugar-sweetened beverage (SSB) consumption compared to different amounts or water
    - Children: 46 articles
      - RCTs: 2 articles
      - NRCTs: 1 article
      - Prospective cohort studies: 43 articles
    - Adults: 27 articles
      - RCTs: 3 articles
      - NRCTs: 1 article
      - Prospective cohort studies: 23 articles
  - Sugar-sweetened beverage consumption compared to low- or no-calorie sweetened beverages (LNCSB)
    - Children: 2 articles
      - RCTs: 2 articles
    - Adults: 6 articles
      - RCTs: 5 articles
      - Prospective cohort studies: 1 article
- In studies examining SSB intake in children, the majority of studies (~80%) reported a significant effect or association between SSB intake and adiposity, however this was not always consistent within studies that reported multiple outcome measures. There were additional concerns related to risk of bias and generalizability.
- In studies examining SSB intake in adults, the majority of studies (~70%) reported a significant effect or association between SSB intake and adiposity; however, this was not



always consistent within studies that reported multiple outcome measures. The 3 included RCTs had significant risk of bias concerns related to the methodology, particularly around the comparator, and concerns with generalizability.

- Two articles from one RCT addressed the relationship between SSB compared to LNCSB intake in children and there was insufficient evidence to draw a conclusion.
- In studies comparing intake of SSBs and LNCSB in adults, there was inconsistency in findings and in methodology. Of the 5 RCTs, 3 did not find a significant difference between groups, however 2 of these studies had small sample sizes and may have been underpowered. Of the 2 studies that did report a significant effect, there was not a significant effect across all reported outcomes. For example, one study reported differences based on the type of sweetener within LNCSB and the other did not find a difference in weight or BMI between groups, but did report that those who consumed LNCSB were more likely to achieve 5% weight loss.

## Description of the evidence

This systematic review included 152 articles that address the relationship between non-alcoholic beverage consumption and outcomes related to growth, size, body composition, and risk of overweight and obesity, of which 76 articles were specific to the exposure or intervention of SSB. The comparator was defined as a different amount (including no intake) of the same beverage type, water, or the solid form of the beverage type (e.g., drinking apple juice compared to eating an apple). Additionally, for SSB, comparators could include low- or no-calorie sweetened beverages.

Unlike the search range for the other beverage types, which ranged from January 2000 to June 2019, for SSB, the search included peer-reviewed articles published from January 2012 to June 2019. This publication date range was narrowed to avoid overlap with the literature reviewed to inform the systematic review by the 2015 Dietary Guidelines for Americans Scientific Advisory Committee.<sup>xxix</sup> The 2020 Dietary Guidelines Advisory Committee Report<sup>xxx</sup> considers this more recent evidence in relation to the review by the 2015 Dietary Guidelines Advisory Committee.

Studies were included if they were conducted in countries categorized as high or very high on the Human Development Index. Studies with the following designs were included: RCTs, non-randomized controlled trials (NRCTs), prospective and retrospective cohort studies, nested case-control studies, and Mendelian Randomization. Studies were included if the study participants were generally healthy or at risk for chronic disease. Participants ages 2 and above were included. The studies in children and in adults were reviewed and synthesized independently.

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<sup>xxix</sup> Dietary Guidelines Advisory Committee. *Scientific Report of the 2015 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture*. US Department of Agriculture, Agricultural Research Service. <https://health.gov/our-work/food-nutrition/2015-2020-dietary-guidelines/advisory-report>. Published 2015. Accessed April 30, 2020

<sup>xxx</sup> Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

### *Study designs:*

- SSB consumption compared to different amounts or water
  - Children (**Table 14**: Summary of articles examining the relationship between SSB consumption versus different amount or water and growth, size, body composition and risk of overweight and obesity in children)
    - RCTs: 2 articles
    - NRCTs: 1 article
    - Prospective cohort studies: 43 articles
  - Adults (**Table 18**)
    - RCTs: 3 articles
    - NRCTs: 1 article
    - Prospective cohort studies: 22 articles
- SSB consumption compared to low- or no-calorie sweetened beverages
  - Children (**Table 22**)
    - RCTs: 2 articles
  - Adults (**Table 24**)
    - RCTs: 5 articles
    - Prospective cohort studies: 1 article

## **SSB vs different amount or water: Children**

### ***Population***

Included studies were from a variety of high and very high HDI countries, including: the United States, Australia, Belgium, Brazil, Canada, Colombia, Denmark, Germany, Iran, Mexico, the Netherlands, Peru, Portugal, Scotland, and the UK. Based on data from studies that reported race/ethnicity, most participants were non-Hispanic white but there was some race/ethnic diversity.

There was a wide age range. In the literature on children, mean ages ranged from 2 to 15 years old with follow-up times ranging from 16 weeks to 17 years and one cohort that followed-up 30 years later during adulthood.

The majority of the studies did not have recruitment criteria for weight status although some recruited normal weight participants only and others recruited participants with overweight or obesity. Analytic sample sizes ranged from 98 to 15,418.

### ***Intervention/exposure and comparator***

All studies included sugar-sweetened beverages, generally, as the intervention or exposure group. Some studies focused more specifically on regular (non-diet) soda or soft drinks.

In the RCTs, participants were encouraged to reduce consumption of SSBs, usually by replacing with water. In the NRCT, change in SSB intake within a single intervention arm was assessed. The cohort studies examined the outcomes based on differences in SSB intake, either as continuous or categorical data. For categorical data, exposure groups were defined differently across the studies.

### ***Outcomes***

To discern 'healthy growth' from 'excessive growth' in children, weight status (prevalence or incidence of overweight or obesity), BMI and BMI z-scores, and body composition measures such

as waist circumference and body fat, were considered to reflect “adiposity”. To assess ‘healthy growth’ in children, outcomes such as height and lean mass were considered.

The most commonly reported outcome measures in children were BMI measures (either BMI for-age-and-sex or BMI Z-scores) (n=38).<sup>1,15,17,27,41,59,61,62,66,70,83-85,89,95,99-103,105,107,110-112,116,117,119,121,123,124,129,130,132,134,135,139,140</sup> Weight status (i.e., prevalence or incidence of overweight or obesity) was reported in 12 studies.<sup>59,84,85,93,97,109,119,123,128,135,138,141</sup> Body composition measures such as waist circumference and body fat were reported in 21 studies.<sup>1,27,61,66,83-85,89,93,101,107,111,116,117,122,124,129,132,135,139,140</sup> Finally, height and lean mass were reported in 2 studies.<sup>2,101</sup>

## ***Evidence synthesis***

There were 2 RCTs that both showed a positive relationship between SSB intake and adiposity in children. They reported a relationship where a decrease in SSB intake was associated with decreased BMI in 6 month<sup>95</sup> and 1-year<sup>101</sup> long interventions. Both controlled for the majority of key confounders. In Ebbeling et al,<sup>101</sup> the overall significant effect was found to be in the Hispanic subgroup. The effect in this study was attenuated by adding sugar intake to the model, lending credibility to the relationship.

There was 1 NRCT that did not show a relationship between SSB intake and adiposity in children. This study was a multicomponent intervention focused on food and beverage consumed away from home (including but not exclusively SSB) which overall did show a relationship with decreased BMI, but SSB as a mediator was not significant. However, the intervention was also relatively short, at 16-weeks.

Of the 42 observational studies reporting adiposity outcomes, the majority (n=33) showed a positive relationship between SSB intake and some measure of adiposity (BMI, waist circumference or percent body fat) in children; the others did not report any significant associations. One study did not have any adiposity outcomes, but reported no significant relationship between SSB intake and height. The relationship between SSB intake and adiposity was found most frequently with measures of BMI adjusted for age and sex. The cohort studies with the strongest design (i.e., lowest risk of bias) reported an association between SSB intake and adiposity in children. However, within studies reporting multiple outcomes, rarely were the associations between SSB intake and each outcome significant.

Studies ranged in size from 98 to 15,444, in ages from 2-15 years, and with durations from 2 months to 6 years. While a majority of studies were conducted with white populations, there were studies conducted in Latino, Black, Asian and Middle Eastern populations.

Energy intake is an important covariate when interpreting studies on the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity because beverages might displace nutrient-dense foods or add additional energy to the diet. Therefore, findings with and without adjustments for energy intake were extracted and reviewed. Conclusion statements reflect the totality and strength of the evidence considering both approaches. Also, funding sources were documented during data extraction for consideration when reviewing this evidence. Further, publication bias is always a consideration in systematic reviews. This body of evidence includes both large and small studies and includes several studies that only report non-significant findings, therefore publication bias is not a serious concern.

## Assessment of the evidence<sup>xxxi</sup>

The conclusion statement “evidence suggests that higher sugar-sweetened beverage intake is associated with greater adiposity in children” was assigned a grade of **moderate**. As outlined and described below, the body of evidence examining SSB consumption (vs different amount or water) and growth, size, body composition, and risk of overweight and obesity in children was assessed for the following elements when grading the strength of evidence.

**Consistency:** Both of the RCTs and the majority of cohort studies reported an association between SSB intake and adiposity. However, the NRCT and a subset of cohorts did not find a significant association. Further, of the studies that report multiple outcomes, few found significant associations across all reported outcomes.

**Directness:** The studies were designed to directly measure and analyze the relationship between SSB intake and outcomes related to growth, size, and body composition. The population, intervention/exposure, comparators, and outcomes (PICO) of the body of evidence align with the elements outlined *a priori* in the Analytic Framework.

**Precision:** Both RCTs reported a power analysis and were sufficiently powered to detect differences in the outcomes assessed; however there were only 2 studies. While prospective cohort studies reported a small effect size, this was consistent across studies and there were several well-designed cohort studies with large sample sizes (20 studies with  $n > 1,000$ ).

**Generalizability:** All of the controlled trials were conducted in children or adolescents with overweight or obesity. Both RCTs had a mean participant age of 15 years<sup>95,101</sup>; the non-randomized controlled trial was conducted in children aged 7 to 11 years.<sup>83</sup> Of the controlled trials, 1 was conducted in only Chinese-American adolescents from northern California.<sup>95</sup> While a majority of prospective cohort studies were conducted with white populations from the United States and Europe, there were studies conducted in Latino, Black, Asian and Middle Eastern populations. The age spectrum of childhood was well represented with mean baseline ages ranging from 2 to 15 years old.

**Risk of bias:** For the RCTs, there was some risk of bias related to randomization, deviations from intended exposure, and selection of reported results (see **Table 15**, **Table 16**, and **Table 17**). For the cohort studies, not controlling for all key confounders was a concern, although there were 4 studies that did control for all key confounders. There was moderate or serious concern of bias from classification of exposures. This was largely due to the use of non-validated assessment tools and an assessment of frequency of consumption without a measure of intake amount. Several studies had risk of bias related to missing data because there was no information or analysis on non-completers. Selection of reported results was also a concern for risk of bias because studies did not have preregistered data analysis plans.

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<sup>xxxi</sup> A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

## **SSB vs different amount or water: Adults**

### ***Population***

Included studies were from a variety of high and very high HDI countries, including: the United States, Australia, Denmark, Finland, Korea, Mexico, and Spain. Based on data from studies that reported race/ethnicity, most participants were non-Hispanic white but there was some race/ethnic diversity. There was a wide age range. In the literature on adults, mean ages ranged from 22 to 69 years old. Follow-up times ranged from 6 months to 20 years. The majority of the studies did not have recruitment criteria for weight status although some recruited normal weight participants only and others recruited overweight or obese individuals. Analytic sample sizes ranged from 47 to 52,987.

### ***Intervention/exposure and comparator***

All studies included sugar-sweetened beverages as the intervention or exposure group. Some studies focused more specifically on regular (non-diet) soda or soft drinks.

In the RCTs, participants were encouraged to reduce consumption of SSBs, usually by replacing with water. In the NRCT, change in SSB intake within a single intervention arm was assessed. The cohort studies examined the outcomes based on differences in SSB intake, either as continuous or categorical data. For categorical data, exposure groups were defined differently across the studies.

### ***Outcomes***

In adults, weight status (prevalence or incidence of overweight or obesity), BMI, and body composition measures such as waist circumference, body fat, and abdominal adiposity were considered to reflect “adiposity”.

In adults, weight or weight change was the most commonly reported outcome.<sup>22,46,64,87,88,91,114,118,120,125,126,131,133,136</sup> Weight status (i.e., prevalence or incidence of overweight or obesity) was reported in 4 studies<sup>22,31,90,127</sup> and BMI was reported in 7 studies.<sup>31,94,96,105,106,127,137</sup> Body composition measures such as waist circumference and body fat were reported in 12 studies.<sup>23,68,86,88,104,113,118,120,125,131,133,137</sup> And, height and lean mass were reported in 2 studies.<sup>120,137</sup>

### ***Evidence synthesis***

There were 3 RCTs with conflicting data with 2 reporting no association<sup>120,133</sup> and 1 reporting a positive association<sup>137</sup> of SSB intake and markers of adiposity in adults. All studies were between 6 and 9 months in duration. Also, 2 of the 3 studies recruited overweight and obese adults,<sup>120,133</sup> whereas 1 study recruited normal weight young adults.<sup>137</sup> The interventions varied across these studies with 1 study comparing sugar-sweetened soda versus water,<sup>120</sup> 1 comparing no SSB versus usual intake,<sup>137</sup> and 1 comparing any energy-yielding beverage with calories versus an active control with behavior modification such as reading labels, increasing vegetable consumption, etc.<sup>133</sup> Significant limitations existed with Maersk et al<sup>120</sup> (i.e., small sample size, n=10 per group) and Tate et al<sup>133</sup> (i.e., included any energy-yielding beverage; active control with multiple behavioral changes) which reduced the strength of evidence. Further, the only RCT with significant findings had several limitations.<sup>137</sup> Within the group that was instructed not to consume SSBs, 80% stopped drinking soft drinks and industrialized juice and 90% stopped drinking whole milk, making it difficult to attribute changes in weight outcomes to differences in SSB consumption.

specifically. Also, they did not report actual SSB intake, other than having inclusion criteria of consuming  $\geq 12$  oz/day of sweetened beverages. Participants were young healthy nursing students from Mexico, which reduces the generalizability of the findings.

There was 1 NRCT comparing a healthy diet in which SSB is limited to usual diet in young adults.<sup>126</sup> The study reported no association between SSB intake and absolute body weight at 3 and 9-months and no association of SSB intake on change in body weight at 3-months. However, a positive association of SSB intake was observed on the change in body weight at 9-months. This study is limited by the non-randomization of the intervention, self-reported weight measure, and higher risk of bias.

There were 18 large and 5 small ( $<1,000$  participants/study) prospective cohort studies. Across the 23 cohort studies, 16 reported a positive association between SSB intake and at least 1 marker of adiposity in adults. However, there was not consistency across studies in terms of which marker was positively correlated. To note, in Pan et al<sup>46</sup> and Qi et al<sup>127</sup> there were multiple large cohorts (both including data from the Nurse's Health Study, among other cohorts). Qi et al. reported positive associations of SSB and BMI in all cohorts showing a dose-response. Pan et al. reported no association of SSB and weight in any of the cohorts but showed positive associations of SSB and weight when stratified by age and by BMI. In summary, findings from cohort studies were inconsistent in terms of significance, several small cohorts did not report power, and many included self-reported weight outcomes and had high attrition.

Energy intake is an important covariate when interpreting studies on the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity because beverages might displace nutrient-dense foods or add additional energy to the diet. Therefore, findings with and without adjustments for energy intake were extracted and reviewed. Conclusion statements reflect the totality and strength of the evidence considering both approaches. Also, funding sources were documented during data extraction for consideration when reviewing this evidence. Further, publication bias is always a consideration in systematic reviews. This body of evidence includes both large and small studies and includes several studies that only report non-significant findings, therefore publication bias is not a serious concern.

### **Assessment of the evidence<sup>xxxii</sup>**

The conclusion statement “evidence suggests that higher SSB intake is associated with greater adiposity in adults” was assigned a grade of **limited**. As outlined and described below, the body of evidence examining SSB consumption (vs different amount or water) and growth, size, body composition, and risk of overweight and obesity in adults was assessed for the following elements when grading the strength of evidence.

**Consistency:** Of 4 controlled trials, 2 RCTs did not report a significant effect of SSBs on adiposity, while 1 RCT and 1 NRCT did find a significant effect these studies had several limitations. The majority of cohort studies reported at least 1 association between SSB intake and adiposity but results of different outcome measures within a study varied with few finding significant associations across all reported outcomes. Further, a subset of cohorts did not find a

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<sup>xxxii</sup> A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

significant association and of the studies that report multiple outcomes.

**Directness:** There were limitations related to the body of evidence in adults in terms of alignment with the PICO elements determined *a priori*. Three of the 4 controlled trials were interventions in those with overweight or obesity or at risk of weight gain. In Tate et al,<sup>133</sup> participants were asked to replace consumption of any energy-yielding beverage (not just SSB) with water. The comparator group of the Vazquez-Duran RCT was to continue usual intake of SSBs, with no measure of how much they were consuming other than inclusion criteria that participants typically drank 12 or more oz/day.<sup>137</sup> The NRCT was a multicomponent intervention targeting fruit and vegetable consumption, take-out meal consumption, and physical activity levels as well as SSB consumption.<sup>126</sup>

**Precision:** For controlled trials, precision was mostly limited by the small number of studies, one of which had a very small sample size and was likely underpowered. There were several large prospective cohort studies with sample sizes over 1,000 and consistency in the effect size.

**Generalizability:** The controlled trials were limited in generalizability due to the relatively small overall number of participants, most with overweight or obesity, and one study that only included a sample of Mexican nursing students. For prospective cohort studies, there were much larger sample sizes. Most studies took place in the United States and Europe, included those with healthy weight, overweight and obesity, and represented a range of ages from 22 to 69 years.

**Risk of bias:** The RCTs were limited due to concerns of risk of bias related to the randomization, deviations from intended interventions, missing outcome data, and selection of the reported results (see **Table 19**, **Table 20**, and **Table 21**). The cohort studies were limited for a variety of reasons. Several studies did not control for all key confounders. For some studies, the timing of exposure and follow-up did not coincide. Classification of exposure was considered a risk due to the use of non-validated measurement tools and when the exposure was based on frequency without information on amount consumed. In several studies, the exposure was only measured at baseline and therefore may not capture changes to intake over time. Some studies did not provide information or analyses on non-completers. Risk of bias was a concern when the outcome measure was self-reported. Finally, a frequent concern was the lack of a preregistered data analysis plan.

## SSB vs LNCSB: Children

### **Population**

There were 2 papers in children, both from the same RCT.<sup>98,115</sup> This study took place in the Netherlands and included children, approximately 8 years old, who commonly drank SSBs. The analytic sample size was 477.

### **Intervention/exposure and comparator**

In the RCT, children who normally consumed SSBs were provided either 1 8-oz can per day of a non-carbonated SSB or 1 8-oz can of an artificially-sweetened non-carbonated beverage for 18 months.<sup>98,115</sup>

### **Outcomes**

To discern 'healthy growth' from 'excessive growth' in children, weight status (prevalence or incidence of overweight or obesity), BMI and BMI z-scores, and body composition measures such as waist circumference and body fat, were considered to reflect "adiposity". To assess 'healthy

growth' in children, outcomes such as height and lean mass were considered. The study in children reported BMI z-scores, body composition measures, and height.<sup>98,115</sup>

### ***Evidence synthesis***

There were 2 papers from 1 RCT included in the body of evidence for comparing SSBs and LNCSBs on adiposity outcomes in children.<sup>98,115</sup> This study provided children with either a can of a non-carbonated SSB or a can of a non-carbonated LNCSB every day for 18 months. DeRuyter et al<sup>98</sup> found that consuming an SSB everyday compared to a LNCSB resulted in increased BMI z-score, sum of skinfolds, waist-to-height ratio, fat mass (both kg and %), waist circumference, and weight. In the follow-up paper, Katan et al<sup>115</sup> reported the impact of consuming LNCSB compared to SSBs was greater in children with initially higher BMI than children with lower BMI for BMI z-score and waist circumference.

### ***Assessment of the evidence***

Given the data is from 1 trial, evidence in children was too limited to draw a conclusion about a relationship between LNCSB consumption versus SSB consumption and measures of adiposity (see **Table 23**).

## **SSB vs LNCSB: Adults**

### ***Population***

The studies took place in the United States, Denmark, Mexico, and Switzerland. In adults, 4 of 6 studies included participants who were overweight or obese. One RCT included primarily female nursing students from Mexico. There was 1 prospective cohort study that included only healthy women.

### ***Intervention/exposure and comparator***

There were some differences across studies in terms of intervention and comparator, particularly around whether beverages were added to the diet versus replacing usual beverage intake. In adults, the RCTs by Campos et al,<sup>92</sup> Tate et al,<sup>133</sup> and Vazquez-Duran<sup>137</sup> instructed participants to replace SSB intake with LNCSB intake. The RCTs by Higgins et al<sup>108</sup> and Maersk et al<sup>120</sup> provided participants with either an LNCSB or a SSB to consume daily.

The amounts of beverages that were either provided or recommended to be replaced differed across studies. Campos et al<sup>92</sup> and Vazquez-Duran et al<sup>137</sup> recommended replacing all SSBs with LNCSBs, but usual intake of the control group (and thus, amount replaced in the intervention group) differed. Campos et al<sup>92</sup> recruited those who consumed 2 or more 22-oz SSBs per day; Vazquez-Duran et al<sup>137</sup> recruited those who consumed 12-oz or more SSBs per day. Maersk et al<sup>120</sup> provided 1 L/day of sucrose-sweetened soft drink or of artificially sweetened soft drink. Higgins et al<sup>108</sup> provided 1.25-1.75 L/day of test beverage depending on body weight.

Of the 5 RCTs in adults, study duration was either 12 weeks<sup>92,108</sup> or 6 months.<sup>120,133,137</sup>



## **Outcomes**

In adults, weight status (prevalence or incidence of overweight or obesity), BMI, and body composition measures such as waist circumference, body fat, and abdominal adiposity were considered to reflect “adiposity”.

In adults, weight or weight change was reported in 4 studies,<sup>92,108,120,133,136</sup> BMI was reported in 3 studies,<sup>92,108,137</sup> body composition measures such as waist circumference and body fat were reported in 5 studies<sup>92,108,120,133,137</sup> and lean mass was reported in 3 studies.<sup>92,108,120</sup>

## **Evidence synthesis**

There were a total of 5 RCTs and 1 cohort study examining the relationship between SSB and LNCSB on adiposity outcomes in adults.

Three papers reported data on BMI; 1 reported significant findings,<sup>108</sup> the other 2 did not.<sup>92,137</sup> The study by Campos et al,<sup>92</sup> which did not report a significant association, had group sample sizes of 14 (SSB) and 13 (LNCSB) and was of 12 weeks duration. This small sample and short timeframe to measure BMI shifts leaves it underpowered. Compliance was also poorly measured. Another trial that did not show a significant effect of SSB versus LNCSB on adiposity had participants consume diets with SSB or LNCSB, but the quantity of consumption was not fixed and compliance was only checked by questionnaire.<sup>137</sup> Additionally, individuals were placed on iso-energetic diets meaning, if followed, it was a test of metabolic effects rather than changes of energy intake. The trial that did find significant effects reported differences by type of LNCS (saccharine, aspartame, rebaudioside-A, sucralose).<sup>108</sup> This trial had participants consume specific LNCSB or SSB for 12 weeks and used para-aminobenzoic acid as a measure of compliance. One LNCSB (saccharine) led to an increase in BMI similar to SSB, while the other 3 LNCSB resulted in no significant change in BMI over the 12 weeks. Thus, the scientifically strongest study led to mixed findings and the weaker studies to no association.

Four papers reported data on body fat. Three of these also reported BMI<sup>92,108,137</sup> and results were similar to those for body fat (2 found no effect, 1 found mixed effects). One additional study had a small sample size with group sizes of 10 (SSB) and 12 (LNCSB).<sup>120</sup> Thus, it had low power and reported no significant association.

Two studies reported data on waist circumference; neither found a difference between SSB and LNCSB. The study by Vazquez-Duran et al<sup>137</sup> had no defined level of intervention and poor compliance testing while the Tate et al<sup>133</sup> study was a weight loss trial of sufficient size, replacing 2 servings/day of SSB with LNCSB.

There were 4 studies reporting effects of SSB versus LNCSB on body weight. Two under-powered studies (all groups n<14) reported no association.<sup>92,120</sup> One stronger study reported an increase in body weight for 1 LNCSB, no change for 2 LNCSB and one decrease relative to sucrose.<sup>108</sup> Another study reported no association with body weight, but the LNCSB group was more likely to achieve a 5% weight loss.<sup>133</sup>

The one cohort study was relatively small (n=170), was 100% female and involved a substitution of one 250-ml serving of LNCSB/day and assessed intake only at baseline. It found lower weight gain with the LNCSB but, with adjustment for TEI, this was not significant.

Energy intake is an important covariate when interpreting studies on the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity because beverages might displace nutrient-dense foods or add additional energy to the diet.

Therefore, findings with and without adjustments for energy intake were extracted and reviewed. Conclusion statements reflect the totality and strength of the evidence considering both approaches. Also, funding sources were documented during data extraction for consideration when reviewing this evidence. Further, publication bias is always a consideration with reviews; however, it is not a serious concern for this body of evidence because multiple studies reported only non-significant findings while others reported significant findings or a mix of significant and non-significant.

### **Assessment of the evidence**<sup>xxxiii</sup>

The conclusion statement “evidence suggests no association between SSB consumption compared with LNCSB on adiposity in adults” was assigned a grade of **limited**. As outlined and described below, the body of evidence examining SSB vs LNCSB consumption in adults and growth, size, body composition, and risk of overweight and obesity was assessed for the following elements when grading the strength of evidence.

**Consistency:** Of the 5 RCTs, 2 papers reported at least one significant effect on adiposity outcomes and 3 papers did not report a significant difference in outcomes between participants who consumed SSBs and those who consumed LNCSB. Of the 2 papers that reported an effect, Higgins et al<sup>108</sup> noted differences based on the type of LNCS. For example, there was no difference in weight or BMI after the 12-week intervention between those who consumed a SSB and a saccharin-sweetened beverage, however weight and BMI were greater in those who consumed SSB compared to beverages sweetened with aspartame, rebaudioside-A, or sucralose. In the RCT by Tate et al,<sup>133</sup> there was no difference in weight or waist circumference between groups after a 6-month intervention, but those that consumed LNCSB were significantly more likely to achieve 5% weight loss. Two of the studies that reported no effect on any outcome had small sample sizes and were likely to be underpowered.<sup>92,120</sup> The single cohort study reported those that consumed SSBs had higher weight compared to those who consumed LNCSB at a 4-year follow up; however, when energy intake was adjusted for, this was no longer significant.<sup>136</sup>

**Directness:** The studies were designed to directly measure and analyze the relationship between sugar-sweetened beverage intake and outcomes related to growth, size, and body composition. The population, intervention/exposure, comparators, and outcomes (PICO) of the body of evidence align with the elements outlined *a priori* in the Analytic Framework.

**Precision:** Samples sizes of the RCTs ranged from 10 and 12 per arm<sup>120</sup> to 105 per arm.<sup>133</sup> Two of the 5 RCTs had group sample sizes ≤14. The single prospective cohort study had an analytic sample of 170.

**Generalizability:** Generalizability was limited due to the small number of participants. The majority of studies in adults were in individuals with overweight and obesity; only one RCT and one cohort study included those of healthy weight status. This RCT was conducted in Mexican nursing students who were predominantly female and the cohort study was only in women,

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<sup>xxxiii</sup> A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

further reducing generalizability.

**Risk of bias:** There were concerns of risk of bias related to the randomization (see **Table 25** and **Table 26**). In one study risk of bias was high for randomization because there were baseline differences between groups.<sup>120</sup> There were some concerns related to deviations from intervention, missing outcome data, and no preregistered data analysis plan. Further, there was little evidence of adherence and short follow-up times.

## Research recommendations

To address the limitations of this body of evidence, several research recommendations have been identified:

- Trials that give participants a particular beverage as the intervention should give the control group a different beverage to test the effect of substituting one beverage for another.
- Studies examining the relationship between beverage consumption and health outcomes should compare intake of particular beverages to intake of water or another comparator
- Differentiate between SSB and LNCSB (cleanly separate the two)

**Table 14: Summary of articles examining the relationship between SSB consumption versus different amount or water and growth, size, body composition and risk of overweight and obesity in children<sup>xxxiv</sup>**

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
CONTROLLED TRIALS			

<sup>xxxiv</sup> Abbreviations: adj: adjusted; BF: body fat; BMI: body mass index; BMIZ: BMI z-score; CDC: Center for Disease Control and Promotion; CI: confidence interval; Cpm: activity counts per minute; d: day(s); DXA or DEXA: dual-energy X-ray absorptiometry; FFQ: food frequency questionnaire; HHS: United States Department of Health and Human Services; MZ: monozygotic; NA: not applicable; NCI: National Cancer Institute; NHLBI: National Heart, Lung, and Blood Institute; NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases; NIH: National Institutes of Health; NR: not reported; NRCT: non-randomized controlled trial; OR: odds ratio; RCT: randomized controlled trial; SD: standard deviation; SE: standard error; SES: socioeconomic status; SKF: triceps and subscapular skinfold thickness; SSB: sugar-sweetened beverage; SSSD: sugar sweetened carbonated soft drinks; Σ4SF: sum of 4 skinfold thicknesses; T: tertile; TBFM: total body fat mass; TEI: total energy intake; unadj; unadjusted; WC: waist circumference; WHO: World Health Organization; wk: week(s); y: year(s)  
 Red font indicates a statistically significant detrimental relationship, and green font indicates a statistically significant beneficial relationship.

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Altman, 2015<sup>83</sup></b>  <b>NRCT, United States</b>  Baseline N=241, Analytic N= 170 for BMIZ, 113 for body fat; Attrition: 29%, 53%; Power: NR</p> <p><b>Recruitment:</b> through local media outlets, schools, organizations, pediatrician referrals, weight-management clinics and word-of-mouth</p> <p><b>Participant characteristics: overweight and obese children aged 7-11y</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 61%</li> <li>• Age: 9.4 (1.2) y</li> <li>• Race/ethnicity: 63% Non-Hispanic white, 17% non-Hispanic black</li> <li>• SES: 43.8 (10.4); Range: 10-65</li> <li>• Anthropometrics: BMIZ ~2.16; Body fat: ~45%</li> <li>• Physical activity: moderate-vigorous, ~47min</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  After a 16-week family-based multicomponent intervention in children with overweight and obesity, BMIZ and body fat decreased; however, this was not associated with changes in SSBs consumed away from home.</p>	<p><b>Intervention: SSB intake</b>  Family-based multi-component, behavioral weight-loss intervention that targets both dietary and physical activity modifications. Participants are encouraged to follow a low-energy-density diet by decreasing consumption of high-energy-dense and low-nutrient foods and increasing consumption of low-energy-dense and high nutrient foods; encouraged to decrease consumption of food away from home</p> <p><b>Comparator:</b> Change in SSB intake, (continuous; svg/d)  <b>Intervention duration:</b> 16wk  <b>Intervention compliance/ diet assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, After 16-wk behavior weight-loss treatment</li> <li>• 3d-24hr recalls completed by parent with assistance from child if present</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Habitual</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, after 16-wk behavior weight-loss treatment</li> <li>• Weight and height measurements were taken in light clothing with shoes removed on a calibrated electronic scale and stadiometer</li> <li>• BMI and BMIZ calculated according to age and sex based on CDC growth curves using the LMS method</li> <li>• Body fat (%) assessed via whole-body dual-energy x-ray absorptiometry</li> </ul>	<p><b>Results of multicomponent intervention (not specific to SSB):</b>  <b>BMIZ (n=170):</b> Baseline, After 16wk multi-component intervention, Mean (SD) <b>2.16 (0.39), 1.87 (0.56), P&lt;0.001</b>  <b>Body fat (%) (n=113):</b> Baseline, After 16wk multi-component intervention, Mean (SD) <b>44.6 (6.5), 40.8 (8.0), P&lt;0.001</b></p> <p><b>Specific to SSB:</b>  <b>Change in percent body fat (n=167):</b>  <b>By change in proportion of energy consumed from food prepared away from home, SSB svg/d, Linear regression, <math>\beta</math>:</b>  0.241, P=0.122</p>	<p>TEI adjusted: Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Study site</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Randomization and allocation methods NR</li> <li>• No power calculation</li> <li>• High attrition/missing data at 16wk</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding Source:</b>  NIH</p>

**Chen, 2019<sup>95</sup>**

**RCT, “iStart Smart for Teens”  
program, United States**

Baseline N= 40, Analytic N= NR;  
Attrition: NR; Power: a total of 40  
adolescent participants in the study, we  
have an 80% chance of detecting a  
larger effect size (.90) between the two  
groups as significant at the 5%

**Recruitment:** recruited at two  
community clinics in northern CA that  
have large Chinese American patient  
populations

**Participant characteristics:  
overweight or obese Chinese-  
American adolescents**

- Total energy intake: kcal/d
- Sex (female): 43%
- Age: 14.9 (1.67) y
- Race/ethnicity: 100% Chinese  
American
- SES: 95% annual family income  
<\$40k
- Anthropometrics: BMI ~28 kg/m<sup>2</sup>;  
BMI% 94.03 (3.59)%
- Physical activity: ~2.3 d/wk of being  
active >60 min
- Smoking: NR

**Summary of findings:**

In a 6mo multicomponent intervention  
among overweight and obese  
adolescents, decreased soda intake was  
associated with decreased BMIZ but not  
significantly associated with change in  
BMI.

**Intervention:** included 3 major  
components, participants (1) used a  
wearable sensor (Fitbit Flex) for 6mo, (2)  
reviewed eight online educational modules  
for 3mo, and, after completing the modules,  
(3) received tailored, biweekly text  
messages for 3mo; intake of sugar-  
sweetened drinks (sweetened drinks,  
sports drink, or energy drinks) based on 2  
questions from validated California Health  
Interview Survey; n=23

**Comparator:** control group participants  
were given a pedometer and a blank food-  
and-activity diary; the adolescents were  
asked to record and track physical activity,  
sedentary activity, and food intake in the  
diary for 3mo and were asked to access  
an online program that consisted of eight  
modules related to general adolescent  
health issues (e.g., diet and nutrition,  
dental care, safety, common dermatology  
care, and risk-taking behaviors); n=17

Intervention duration: 6mo

Intervention compliance: NR

**Study beverage intake:** svg/d

- Sugar sweetened drink intake ~5.5

**Outcome assessment methods/timing:**

- At baseline, 6mo
- Weight, height, waist-to-hip ratio:  
methods NR
- BMI calculated as kg/m<sup>2</sup>
- Weight status definitions based on  
CDC growth chart: Overweight (BMI  
85<sup>th</sup>-94<sup>th</sup>%); Obese (BMI >95<sup>th</sup>%)

**For intervention group:**

Change in BMI: NS, Data NR

Change in BMIZ:  $\beta$

**Soda consumption: -0.08, P=0.015**

**TEI adjusted:** No

**Confounders accounted for:**

- Key confounders: sex, age,  
race/ethnicity, SES, anthropometry at  
baseline, physical activity
- Other factors considered: N/A

**Confounders NOT accounted for:**

- Key confounders: smoking
- Other factors considered: total energy  
intake, timing, temporal use, sugar,  
protein, fiber, energy density,  
medications, supplements, alcohol

**Additional model adjustments:** N/A

**Limitations:**

- Exposure not well defined
- Compliance NR
- Analytic N/attrition NR
- Trial registry did not include data  
analysis plan to report waist-to-hip  
ratio

**Funding Source:**

American Nurses Foundation Research  
Award

**Ebbeling, 2012<sup>101</sup>**

**RCT, United States**

Baseline N=224, Analytic N=209;  
Attrition: 7%; Power: designed to have  
80% power at a type I error rate of 5% to  
detect a net intervention effect with  
respect to the primary outcome BMI of  
0.49, based on pilot

**Recruitment:** NR

**Participant characteristics:  
overweight adolescents who regularly  
consume  $\geq 1$  serv/d (12oz) of SSB or  
100% fruit juice**

- Total energy intake: ~1935 kcal/d
- Sex (female): 45%
- Age: ~15yo (9-10<sup>th</sup> grade)
- Race/ethnicity: ~55% white, ~20% Hispanic, 24% Black, 4% Asian
- SES: ~40%  $\geq$ \$60K/y
- Anthropometrics: BMI ~30.2; Overweight, ~38%; Obese, ~62%
- Physical activity: ~1.54 MET
- Smoking: NR

**Summary of findings:**

Overweight adolescents in a 1-year intervention that was focused on reducing sugar-sweetened beverage consumption showed a significantly lower increase in BMI and weight after 1 year compared to those in the control group; these differences were no longer significant after a year of follow-up. This effect was largely due to differences between Hispanic and non-Hispanic participants. There were no significant differences in change in height over 2 years between the groups.

**Intervention (n=110):** home delivery of noncaloric beverages (e.g., bottled water and "diet" beverages) every 2 weeks, monthly motivational telephone calls with parents (30 minutes per call), and three check-in visits with participants (20 minutes per visit). Written intervention messages with instructions to drink the delivered beverages and not to buy or drink sugar-sweetened beverages were mailed to participants. Unsweetened water was recommended over artificially sweetened beverages. Discussions during telephone calls and check-in visits focused exclusively on beverage consumption, with no attention to other dietary behaviors or to physical activity

**Comparator (control, n=114):** mailed \$50 supermarket gift cards to participants in the control group at 4 and 8 months as a retention strategy but did not provide instructions on what to purchase with the cards

Intervention duration: 12mo, plus additional 12mo follow-up

Intervention compliance: dietary recall: SSB intake decreased in both groups at 1y and 2y but more so in the intervention group than the control (1y  $P<0.001$ ; 2y  $P=0.005$ )

**Study beverage intake:**

- SSB: ~1.7 sv/d

**Outcome assessment methods/timing:**

- At baseline, after 1y intervention, after additional 1y follow-up
- Weight and height: measured by trained personnel using calibrated scales and stadiometers
- Body fat, %: used data from bioelectrical impedance analysis (BIA) and the equation of Sun et al.

**BMI change from baseline: between group differences, mean (SD); 1y, 2y**  
**All participants: -0.57 (0.28),  $P=0.045$**   
(Note: when sugar added to model, -0.39,  $P=0.24$ );  
-0.30 (0.40),  $P=0.46$   
**Non-Hispanic participants: -0.29 (0.31),  $P=0.36$ ; 0.18 (0.44),  $P=0.68$**   
**Hispanic participants: -1.79 (0.65),  $P=0.007$ ; -2.35 (0.92),  $P=0.01$**

**Weight change from baseline: between group differences, mean (SD); 1y, 2y**  
**All participants: -1.9 (0.9),  $P=0.04$ ; -0.8 (1.4),  $P=0.55$**   
**Non-Hispanic participants: -0.8 (1.0),  $P=0.42$ ; 1.1 (1.5),  $P=0.48$**   
**Hispanic participants: -6.4 (2.1),  $P=0.003$ ; -8.8 (3.1),  $P=0.005$**

**Height change from baseline: between group differences, mean (SD); 1y, 2y**  
**All participants: -0.2 (0.2),  $P=0.49$ ; 0.2 (0.4),  $P=0.67$**   
**Non-Hispanic participants: -0.1 (0.3),  $P=0.80$ ; 0.4 (0.4),  $P=0.29$**   
**Hispanic participants: -0.6 (0.6),  $P=0.30$ ; -1.0 (0.8),  $P=0.24$**

**Body fat, %, change between groups:**  
-0.5 (0.6),  $P=0.40$

[Note: data on within-group differences can be found in the paper. Overall, BMI, weight, and height all increased significantly within both groups from baseline to 2y.]

**TEI adjusted:** Yes

**Energy Intake, kcal/d, Mean (SD): 1y, 2y**  
Experimental: -454 (48),  $P<0.001$ ;  
-361 (54),  $P<0.001$   
Control: -176 (48),  $P<0.001$ ;  
-178 (54),  $P=0.001$   
Difference: -278 (69),  $P<0.001$ ;  
-183 (76),  $P=0.02$

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity
- Other factors considered: total energy intake, sugar

**Confounders NOT accounted for:**

- Key confounders: smoking
- Other factors considered: timing, temporal use, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:**  
N/A

**Limitations:**

- Randomization and allocation methods NR
- Discrepancy in frequency and type of contact between intervention and control groups
- No preregistered data analysis plan

**Funding Sources:**

NIDDK; National Center for Research Resources to the Boston Children's Hospital General Clinical Research Center; Harvard Catalyst Clinical and Translational Science Center; New Balance Foundation

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<b>PROSPECTIVE COHORT STUDIES</b>			
<p><b>Alviso-Orellana, 2018<sup>84</sup></b></p> <p><b>Prospective Cohort Study, Young Lives cohort study, Peru</b> Baseline N=1942, Analytic N=1813; Attrition: 7%; Power: NR</p> <p><b>Recruitment:</b> multistage, cluster-stratified, random sampling technique; oversampled poor areas</p> <p><b>Participant characteristics: normal weight children at high-risk of overweight</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49%</li> <li>Age: ~8y</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: 22% overweight; WC= ~61cm</li> <li>Physical activity: none=9%; daily=33%</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b> In poor areas of Peru, drinking SSBs daily compared to never was associated with greater incidence of becoming overweight, as well as higher weight and BMI 4 years later. There was no significant association between frequency of SSB intake and WC.</p>	<p><b>Exposure of interest:</b> SSBs ("fizzy, sweet soft drinks such as sodas"). Authors noted that "question used to assess sweetened beverage consumption was not specific to sodas, but potentially included diet sodas, sports drinks, etc."</p> <p><b>Comparators:</b> SSB intake, categorical:</p> <ul style="list-style-type: none"> <li>Never (ref)</li> <li>Up to every 2 wk</li> <li>2-6 times/wk</li> <li>Daily</li> </ul> <p>Other exposure measures: N/A</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Maternal report questionnaire; representing intake over last 30d</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSB: never=13%, daily=3%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 4y follow-up</li> <li>Overweight based on BMI and the International Obesity Task Force's sex- and age- specific BMI cut-off points were used</li> <li>Waist and abdominal circumference (methods NR)</li> </ul>	<p><b>Incidence of overweight</b> (n=1414), RR (95% CI) Never (ref) Up to every 2 wk: 1.15 (0.66, 1.99) 2-6 times/wk: 1.34 (0.80, 2.25) <b>Daily: 2.12 (1.05, 4.28), P&lt;0.05</b></p> <p><b>Weight</b>, kg, <math>\beta</math> (95% CI) Never (ref) Up to every 2 wk: 0.58 (-0.22, 1.37) 2-6 times/wk: 0.55 (-0.21, 1.32) <b>Daily: 2.29 (0.62, 3.96), P&lt;0.05</b></p> <p><b>BMI</b>, kg/m<sup>2</sup>, <math>\beta</math> (95% CI) Never (ref) Up to every 2 wk: -0.08 (-0.39, 0.24) 2-6 times/wk: 0.14 (-0.15, 0.43) <b>Daily: 0.74 (0.15, 1.33), P&lt;0.05</b></p> <p><b>WC</b>, cm, <math>\beta</math> (95% CI) Never (ref) Up to every 2 wk: 0.16 (-0.64, 0.96) 2-6 times/wk: 0.80 (-0.01, 1.61) Daily: 1.43 (-0.41, 3.27)</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, physical activity</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, anthropometry at baseline, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Mother's overweight status</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure data only measured at baseline</li> <li>Exposure data collection tool not validated</li> <li>Exposure is frequency of SSB intake, does not account for amount of intake</li> <li>Outcome assessment methods NR</li> <li>No preregistered data analysis plan</li> <li>Peru is considered high HDI as of 2005; however this study excluded wealthiest areas and oversampled poor areas (generalizability)</li> </ul> <p><b>Funding source:</b> Wellcome Trust Research Training Fellowship in Public Health and Tropical Medicine</p>



# Ambrosini, 2013<sup>85</sup>

## Prospective Cohort Study, Western Australian Pregnancy Cohort (Raine) Study, Australia

Baseline N=1830, Analytic N=1009;  
Attrition: 45%; Power: NR

**Recruitment:** pregnant women from hospitals and clinics in Western Australia

### Participant characteristics: adolescents

- Total energy intake: ~9.7 MJ
- Sex (female): ~48%
- Age: 14y
- Race/ethnicity: NR
- SES: NR
- Anthropometrics: BMI ~21.3; WC: ~75cm
- Physical activity: Physical fitness ~110 watts
- Smoking: NR

**Summary of findings:** In girls, there was a significant association between higher SSB intake at age 17y compared to age 14 and greater odds of overweight or obesity and greater increases in BMI. There was no significant association between SSB intake and WC in girls. In boys, greater SSB intake was associated with increases in WC, but not change in BMI or odds of overweight or obesity.

**Exposure of interest:** SSB, daily intake (g/d), includes all carbonated (soft) drinks, cordials or squash (fruit drink concentrate), and fruit juice drinks (with the exclusion of 100% juice); does not include artificially sweetened or diet drinks (1 svg= 1c= 250mL= 261g)

**Comparators:** SSB intake (categorical, svg/d), Tertiles

- Tertile 1: 0–0.5 svg/d (0–130 g/d)
- Tertile 2: 0.5–1.3 svg/d (130–329 g/d)
- Tertile 3: >1.3 svg/d (331–2876 g/d)

Other exposure measures: n/a

### Exposure assessment method and timing:

- Validated semi-quantitative FFQ, included frequency of consumption and portion sizes; represents usual dietary intake over the previous year (at 14y, parents assisted)
- Baseline (14yo), 3y follow-up (17yo)

**Study beverage intake:** g/d, Mean (SD)

- SSB intake:
  - Tertile 1: 48 (37)
  - Tertile 2: 224 (58)
  - Tertile 3: 651 (321)

### Outcome assessment methods/timing:

- Baseline, 3y follow-up (17yo)
- Height and weight: calibrated measurements made using electronic chair scales and a stadiometer
- Overweight and obesity defined using International Obesity Task Force cutoffs for BMI
- Waist circumference (WC) measured at the level of the umbilicus to the nearest 0.1 cm, and the average of 2 measurements was used

**Odds of overweight or obesity,** OR (95%CI)

### Girls (n=624):

Tertile 1: (ref)

Tertile 2: 1.1 (0.5, 2.5), P=0.75

**Tertile 3: 3.8 (1.5, 9.3), P=0.004**

**P-trend: 0.005**

### Boys (n=680):

Tertile 1: (ref)

Tertile 2: 1.5 (0.6, 3.3), P=0.37

Tertile 3: 0.8 (0.3, 2.1), P=0.76

P-trend: 0.72

**BMI,** % of change (95%CI)

### Girls (n=660):

Tertile 1: (ref)

Tertile 2: 0.4 (-1.3, 2.1), P=0.64

**Tertile 3: 3.6 (1.5, 5.8), P=0.001**

**P-trend: 0.002**

### Boys (n=706):

Tertile 1: (ref)

Tertile 2: 0.3 (-1.6, 2.3), P=0.75

Tertile 3: 0.8 (-1.3, 2.9), P=0.46

P-trend: 0.46

**WC,** % of change (95%CI)

### Girls (n=656):

Tertile 1: (ref)

Tertile 2: 0.8 (-0.1, 1.7), P=0.08

Tertile 3: 0.9 (-0.2, 2.0), P=0.09

P-trend: 0.07

### Boys (n=704):

Tertile 1: (ref)

**Tertile 2: 1.3 (0.3, 2.2), P=0.011**

**Tertile 3: 1.4 (0.2, 2.3), P=0.019**

**P-trend: 0.025**

**TEI adjusted:** No, but adjusted for dietary pattern score

### Confounders accounted for:

- Key confounders: sex, age, SES, anthropometry at baseline, physical activity
- Other factors considered: N/A

### Confounders NOT accounted for:

- Key confounders: race/ethnicity, smoking
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:** Pubertal stage, dietary misreporting, healthy and Western dietary pattern scores

### Limitations:

- Not all key confounders accounted for
- Attrition >45% with no information on non-completers
- No preregistered data analysis plan

### Funding sources:

National Heart Foundation of Australia and Beyond Blue Cardiovascular Disease and Depression Strategic Research Program; Australian National Health and Medical Research Council; UK Medical Research Council

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Bigornia, 2015<sup>89</sup></b></p> <p><b>Prospective Cohort Study, Avon Longitudinal Study of Parents and Children (ALSPAC), UK</b></p> <p>Baseline N=14541, Analytic N=2455; Attrition: 83%; Power: NR</p> <p><b>Recruitment:</b> pregnant women with expected delivery dates between April 1991 and December 1992 and living in the County of Avon located in South-West England started in 1990</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: ~1900 kcal/d</li> <li>Sex (female): 53%</li> <li>Age: ~10.6y</li> <li>Race/ethnicity: NR</li> <li>SES: mothers, college degree or higher: ~50%</li> <li>Anthropometrics: BMI ~17.5; ~21% ovwt/obese; WC: ~63cm</li> <li>Physical activity: ~500 counts/min (accelerometer)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>An increase in SSB consumption from age 10 to 13 was associated with increases in weight, BMI, waist circumference, and body fat at age 13 when energy intake was not adjusted for.</p>	<p><b>Exposure of interest:</b> SSB (full-sugar fruit squashes, cordials and fizzy drinks (i.e. soda) with added sugar; Not including reduced-sugar or artificially sweetened beverages); 1 svg=180g</p> <p><b>Comparators:</b> SSB, continuous</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>3d dietary record completed by children with parental assistance, reviewed by fieldworker</li> <li>At ages 10, 13y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSB: ~60% consumers at baseline; ~0.35 svg/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At ages 10, 11, 13y</li> <li>Weight measured using Tanita body fat analyser</li> <li>Height measured using a Harpenden stadiometer</li> <li>BMI was calculated as kg/m<sup>2</sup></li> <li>Overweight/obese: BMI≥25 kg/m<sup>2</sup> based on International Obesity Task Force age- and sex-specific categories</li> <li>Waist circumference (WC) measured at the midpoint between the lowest rib and the top of the iliac crest</li> <li>Total body fat mass (TBFM) measured with DXA using a Lunar Prodigy narrow fan beam densitometer</li> </ul>	<p><b>Change of SSB intake from ages 10-13y on adiposity outcomes at 13y (n=1059), <math>\beta</math></b></p> <p><b>Weight (kg):</b> <b>Unadj TEI: 0.066, P=0.001;</b> Adj TEI: attenuated by 47%, Data NR</p> <p><b>BMI (kg/m<sup>2</sup>):</b> <b>Unadj TEI: 0.074, P&lt;0.001</b> Adj TEI: attenuated by 25%, Data NR</p> <p><b>WC (cm):</b> <b>Unadj TEI: 0.097, P&lt;0.001</b> Adj TEI: attenuated by 22%, Data NR</p> <p><b>TBFM (kg):</b> <b>Unadj TEI: 0.065, P=0.003</b> Adj TEI: remained similar, Data NR</p> <p><b>Change of SSB intake from ages 10-13y on WC at 13y, adjusting for adiposity, <math>\beta</math></b> <b>WC, adjusting for BMI: 0.042, P=0.02</b> <b>WC, adjusting for TBFM: 0.048, P=0.01</b></p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Pubertal stage at 13y, maternal overweight/obesity status, dieting at age 13 years, and change in fruit juice, fruit and vegetable, and total fat intakes from age 10-13y</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure data collection tool not validated</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b> UK Medical Research Council; Wellcome Trust; University of Bristol; American Diabetes Association</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Cantoral, 2016<sup>93</sup></b></p> <p><b>Prospective Cohort Study, Early Life Exposure in Mexico to Environmental Toxicants (ELEMENT) project &amp; Formative Children's Environmental Health (CEH) Centre, Mexico</b></p> <p>Baseline N= 250, Analytic N=227; Attrition: 9%; Power: NR</p> <p><b>Recruitment:</b> convenience sample</p> <p><b>Participant characteristics at revisit stage (age 8-14y): children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: 2637 (844) kcal/d</li> <li>Sex (female): 54%</li> <li>Age: 8-14y</li> <li>Race/ethnicity: NR</li> <li>SES: 94% monthly family income level &lt;\$35000 Mexican pesos (~\$2333 USD)</li> <li>Anthropometrics: 22% Obesity, 19% Waist circumference &gt;90<sup>th</sup>%</li> <li>Physical activity: 5.8 (3.3) hr/wk</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>Children in the highest tertile of SSB consumption from age 1 to 5y had significantly greater odds of obesity and abdominal obesity at ages 8-14y compared with those in the lowest tertile. There was not a significant association between age of introduction of SSB (before versus after 12 mo) and odds of obesity or abdominal obesity.</p>	<p><b>Exposure of interest:</b> SSBs (sodas, commercial fruit drinks and flavored water with sugar; not including natural fruit or vegetable juices)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Initiation of SSBs: ≤12mo, &gt;12mo (ref)</li> <li>Cumulative consumption of SSBs, ages 1-5y: tertiles <ul style="list-style-type: none"> <li>T1: 1642–15,242 mL</li> <li>T2: 15,410–22,484 mL</li> <li>T3: 22,731–55,913 mL</li> </ul> </li> </ul> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Validated semi-quantitative FFQ; estimates intake over previous 3mo</li> <li>At baseline (age 12mo), every 6mo, and at "revisit" stage (age 8-14y)</li> </ul> <p><b>Study beverage intake:</b> mL/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>SSB intake at revisit stage: 421 (352)</li> <li>73% introduced to SSBs &lt;12mo of age</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At revisit stage (age 8-14y)</li> <li>Weight measured by trained personnel with a Bame scale</li> <li>Height measured by trained personnel with a stadiometer</li> <li>Waist circumference measured by trained personnel using a measuring tape</li> <li>'Obese': &gt;2 SD of BMIZ, according to WHO</li> <li>Abdominal obesity: Waist circumference ≥ 90th percentile for age and sex</li> </ul>	<p><b>Odds of Obesity (&gt;2SD BMIZ) at age 8-14y by SSB intake from age 1-5y, OR (95% CI)</b></p> <p><b>Age of introduction of SSBs:</b></p> <ul style="list-style-type: none"> <li>&gt;12 mo: ref</li> <li>≤12mo: 2.00 (0.87, 4.59)</li> </ul> <p><b>Cumulative SSB intake (1-5y):</b></p> <ul style="list-style-type: none"> <li>T1: ref</li> <li>T2: 0.84 (0.32, 2.13)</li> <li><b>T3: 2.99 (1.27, 7.00)</b></li> </ul> <p><b>P-trend=0.01</b></p> <p><b>Odds of Abdominal obesity (WC&gt;90%) at age 8-14y by SSB intake from age 1-5y, OR (95% CI)</b></p> <p><b>Age of introduction of SSBs:</b></p> <ul style="list-style-type: none"> <li>&gt;12 mo: ref</li> <li>≤12mo: 1.70 (0.70, 4.09)</li> </ul> <p><b>Cumulative SSB intake (1-5y):</b></p> <ul style="list-style-type: none"> <li>T1: ref</li> <li>T2: 1.14 (0.42, 3.07)</li> <li><b>T3: 2.70 (1.03, 7.03)</b></li> </ul> <p><b>P-trend: 0.03</b></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES, anthropometry at baseline, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b></p> <p>Any breastfeeding up to 12 mo, maternal obesity at 12mo postpartum, TV watching</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Follow-up time may differ among participants</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>US NIEHS; Consejo Nacional de Ciencia y Tecnologia (CONACyT); NIEHS/US EPA Formative Children's Center for Environmental Health and Disease Prevention Research</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Carlson, 2012<sup>66</sup></b>  <b>Prospective Cohort Study, MOVE Project (RCT), United States</b>  Baseline N=271, Analytic N=254 (Attrition: 6%); Power: NR</p> <p><b>Recruitment:</b> public recreation centers in San Diego County, California</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 56%</li> <li>• Age, Mean (SD): 6.7 (0.7) y</li> <li>• Race/ethnicity: 48% Latino, 39% non-Hispanic white</li> <li>• SES: Parent had college degree 41%</li> <li>• Anthropometrics: BMI: ≥85<sup>th</sup> 20%, ≥95<sup>th</sup> 15%; Body Fat %, Mean (SD)=29.9 (8.7)</li> <li>• Physical activity: 4.35 (2.00) days/wk</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, SSB intake was significantly associated with increased percent body fat at 24mo follow-up, but was not associated with BMIZ.</p>	<p><b>Exposure of interest:</b> SSB (soda, not diet (12oz); Hawaiian Punch, fruit drinks, lemonade, sugar-sweetened ice tea, Tampico, or other noncarbonated sugary drinks (8oz); sports drinks like Gatorade or Powerade (12oz))</p> <p><b>Comparator:</b> SSB intake (continuous; svg/d)</p> <p>Other exposure measures: 100% fruit or vegetable juice</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Unvalidated survey completed by parents; represents usual dietary behavior</li> <li>• At baseline, and 24mo follow-up</li> </ul> <p><b>Study beverage intake:</b> svg/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>• SSB intake: 0.54 (0.59)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, and 24mo follow-up</li> <li>• Height and weight measured by trained staff</li> <li>• Age- and gender-specific BMI percentiles and z-scores (BMIZ) calculated using CDC growth charts</li> <li>• Percent body fat measured using bioelectrical impedance analysis and Schaefer equation</li> </ul>	<p><b>BMIZ</b>, Linear regression, B (95% CI)  <b>Change per svg/d increase:</b>  0.11 (-0.03, 0.25), P=0.124</p> <p><b>Percent Body Fat</b>, Linear regression, B (95% CI)  <b>Change per svg/d increase:</b>  <b>1.40 (0.09, 2.72), P=0.036</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Baseline height</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Exposure measured using unvalidated method</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NIDDK</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>DeBoer, 2013<sup>99</sup></b></p> <p><b>Prospective Cohort Study, Early Childhood Longitudinal Survey—Birth cohort (ECLS-B), United States</b></p> <p>Baseline N=7600, Analytic N=6800; Attrition: 11%; Power: NR</p> <p><b>Recruitment:</b> a random sampling of &gt;14,000 birth certificates</p> <p><b>Participant characteristics: young children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 49%</li> <li>• Age: 2y</li> <li>• Race/ethnicity: 43% White, 21% Hispanic, 15% Black, 10% Asian</li> <li>• SES: 44% High/Medium High</li> <li>• Anthropometrics: 91% Normal weight</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>Regular SSB consumption at age 2 was significantly associated with a greater increase in BMIZ between ages 2 and 4 years. There was no significant association between SSB at age 4 and change in BMIZ between ages 4 and 5 years.</p>	<p><b>Exposure of interest:</b> SSB intake (soda pop, for example, Coke, Pepsi, or Mountain Dew; sports drinks, for example, Gatorade; fruit drinks that are not 100% fruit juice, for example, Kool-Aid, Sunny Delight, Hi-C, Fruitopia, or Fruitworks); 8oz=1glass</p> <p><b>Comparators:</b> SSB consumption categorical</p> <ul style="list-style-type: none"> <li>• <b>SSB regular drinker:</b> at 2y, child usually drinks SSBs with meals and/or snacks; at 4 and 5y, drink ≥1 serving of SSB daily</li> <li>• <b>SSB infrequent/nondrinker:</b> at 2y, child does not usually drink SSBs with meals and/or snacks; at 4 and 5y, drink &lt;1 serving of SSB daily</li> </ul> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Primary caregiver completed a computer-assisted interview; not validated</li> <li>• At ages 2, 4, and 5y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• SSB consumption: &lt;1 svg/d: 91%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At ages 2, 4, and 5y</li> <li>• Height and weight were obtained by trained researchers by using a standardized protocol</li> <li>• BMI calculated as kg/m<sup>2</sup></li> <li>• Age- and gender-specific BMI z-scores (BMIZ) calculated based on 2000 CDC growth charts</li> <li>• Normal weight: up to 85th percentile</li> <li>• Overweight: &gt;85th to 95th percentile</li> <li>• Obese: &gt;95th percentile</li> </ul>	<p><b>BMIZ:</b> Linear regression</p> <p><b>SSB at 2y and change in BMIZ from 2-4y:</b></p> <p>&lt;1 svg/d (ref)</p> <p>≥1 svg/d: greater increase in BMIZ (Data NR), P&lt;0.05</p> <p><b>SSB at 4y and change in BMIZ from 4-5y:</b></p> <p>Data NR, P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES, anthropometry at baseline,</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No information on non-completers</li> <li>• Exposure data collection tool not validated</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b></p> <p>NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>De Coen, 2014</b><sup>97</sup></p> <p><b>Prospective Cohort Study, Prevention of Overweight among Pre-school and school children (POP-project), Belgium</b></p> <p>Baseline N= 621, Analytic N=473; Attrition: 24%; Power: NR</p> <p><b>Recruitment:</b> In the 3 municipalities, all pre-primary and primary schools were invited to participate; within these schools, all pre-primary children (age 3 to 5 years) and those in the first year of primary school (age 6 years) were invited to participate</p> <p><b>Participant characteristics: young children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 53%</li> <li>Age: 4.95 (1.29) y</li> <li>Race/ethnicity: NR</li> <li>SES: Majority of parents in paid work (86% mothers, 91% fathers)</li> <li>Anthropometrics: 19% Overweight</li> <li>Physical activity: At home 5.98 (2.60) hr/wk, Structured 4.06 (4.72) hr/wk</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In young children, there was no significant association between soft drink intake and odds of being overweight 18 or 30 months later.</p>	<p><b>Exposure of interest:</b> Soft drink intake</p> <p><b>Comparators:</b> categorical, based on mean intake at baseline</p> <ul style="list-style-type: none"> <li>≤65 mL/d</li> <li>&gt;65 mL/d</li> </ul> <p>Other exposure measures: water</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated semi-quantitative FFQ, assessed quantities and frequencies of soft drinks</li> <li>At baseline, 18mo and 30mo follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Soft drink intake: ~65 mL/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 18mo and 30mo follow-up</li> <li>Height and weight measured by research team</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>BMI Z-scores were calculated with Flemish reference data using the LMS</li> <li>Overweight: cut-off point BMIZ=1</li> </ul>	<p><b>Childhood overweight</b> by baseline soft drink consumption &gt;65 ml/d: Logistic regression, OR (95% CI)</p> <p><b>18mo follow-up (n=538):</b> 1.45 (0.85, 2.48) <b>30mo follow-up (n=473):</b> 1.36 (0.77, 2.40)</p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b> Ministry of the Flemish Community</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Dong, 2015<sup>15</sup></b>  <b>Prospective Cohort Study, Avon Longitudinal Study of Parents and Children (ALSPAC), UK</b>  Baseline N=15444 (recruited), Analytic N=4646 (Attrition: 70%) Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49.2%</li> <li>Age: Mean=7.5y</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI, Mean=16.2; BMI z-score, Mean=0.1</li> <li>Physical activity: Mean=22.9 min/d, SD=15.4 (at 11y)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Among children, increases in sugar-sweetened beverages over 3y, was associated with excessive weight gain (increase in BMI z-score); however, there was no significant association between average intake of sugar-sweetened beverages and excessive weight gain over 3y.</p>	<p><b>Exposure of interest:</b> Sugar-sweetened beverages (normal fizzy drinks, made-up squash, normal squashes and cordials)</p> <p><b>Comparators:</b> Sugar-sweetened beverages (continuous; g/d)</p> <ul style="list-style-type: none"> <li>Per 100 g/d change over 3y</li> <li>Per 100 g/d average across 3y</li> </ul> <p>Other exposures: full-fat milk, low-fat milk, juices, diet soda</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Three-day food diary, child report with help from parent; Represents current intake</li> <li>At 7y, 10y, and 13y</li> </ul> <p><b>Study beverage intake:</b> g/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>Sugar-sweetened beverages: <ul style="list-style-type: none"> <li>7y: 82.2 (132.8)</li> <li>10y: 106.9 (155.9)</li> <li>13y: 131.9 (212.8)</li> </ul> </li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At 7y, 10y, and 13y</li> <li>Height and weight measured by study personnel</li> <li>Calculated UK age and sex adjusted BMI z-score to represent adiposity</li> <li>Excessive weight gain: increase in adiposity over 3y compared to reference group</li> <li>BMI converted to g for interpretation (assumes 0.01 increase in BMI z-score = 50g)</li> </ul>	<p><b>Excess weight gain (g) over 3y</b>, per 100 g/d increase (change) or per 100 g/d intake (average), Mean, linear regression</p> <p><b>Sugar-sweetened beverage intake, continuous</b>  <b>Change: B: 35, P&lt;0.05</b>  Average: B: -20, P=NS  <b>Boys (n=2155)</b>  <b>Change: B: 49, P&lt;0.05</b>  <b>Girls (n=2193)</b>  Change: B: 22, P=NS  <b>7-10y period</b>  Change: B: 43, P&lt;0.10  <b>10-13y period</b>  <b>Change: B: 49, P&lt;0.01</b></p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, physical activity</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, anthropometry at baseline, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Puberty status (Tanner stage)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Impact of missing data on analyses unclear</li> <li>Results from subgroup analyses are only report for change data, not average intake data which may show fewer/no significant associations</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NR</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>DuBois, 2016<sup>17</sup></b>  <b>Prospective Cohort Study, Quebec Newborn Twin Study, Canada</b>            Baseline N=1324, Analytic N=304 (Attrition: 77%); Power: NR</p> <p><b>Participant characteristics: monozygotic (MZ) twin children</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean (SD): 1814.37 kcal/d (393.20)</li> <li>Sex (female): 54.6%</li> <li>Age, Mean (SD): 8.96 y (0.56)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics, Mean (SD): BMI, 16.51 (2.50)</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            In MZ twins, there was not a significant association between intrapair differences in sugary drink intake at age 9 and intrapair differences in BMI in subsequent years.</p>	<p><b>Exposure of interest:</b> Sugary drinks</p> <p><b>Comparator:</b> Sugary drinks (kcal), continuous</p> <p>Other exposures: milk, fruit juice, fruit drinks, soft drinks</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>24-hr recall performed by registered dietitians; Represents usual intake</li> <li>At baseline (9y)</li> </ul> <p><b>Study beverage intake, kcal, Mean (SD)</b></p> <ul style="list-style-type: none"> <li>Sugary drinks: 74.22 (81.95)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (9y), 12y, 13y, 14y</li> <li>Height and weight self-reported except at baseline (measured)</li> <li>Intrapair difference (MZ twins) in BMI</li> <li>Discordant twins defined as <math>\geq 2</math> BMI units between pairs at least once at 9, 12, 13, and/or 14y</li> <li>Concordant twins defined as <math>&lt; 2</math> BMI units between pairs at all ages</li> </ul>	<p><b>Sugary drink intake</b>, continuous            Correlation between intrapair differences in intake at 9y (kcal or % energy) and intrapair differences in BMI in subsequent yrs; Spearman correlation  <b>All: kcal; % energy</b>  <b>12y</b> (n=238): -0.02, NS; -0.04, NS  <b>13y</b> (n=226): -0.00, NS; -0.03, NS  <b>14y</b> (n=212): -0.06, NS; -0.05, NS  <b>Change 9-14y</b> (n=210): -0.09, NS; -0.08, NS  <b>Boys: kcal; % energy</b>  <b>12y</b> (n=102): -0.01, NS; 0.01, NS  <b>13y</b> (n=96): 0.12, NS; 0.10, NS  <b>14y</b> (n=92): -0.14, NS; -0.12, NS  <b>Change 9-14y</b> (n=92): -0.17, NS; -0.16, NS  <b>Girls: kcal; % energy</b>  <b>12y</b> (n=136): -0.07, NS; -0.12, NS  <b>13y</b> (n=130): -0.14, NS; -0.17, NS  <b>14y</b> (n=120): 0.01, NS; -0.00, NS  <b>Change 9-14y</b> (n=108): -0.02, NS; -0.04, NS</p> <p><b>Refer to paper and supplemental data for additional analyses on:</b></p> <ul style="list-style-type: none"> <li>Comparison of Dietary Intake (at 9 years) Among Leaner and Heavier Twins From Discordant and Concordant MZ Twin Pairs</li> <li>Comparison of Dietary Intake at 9 Years Between Discordant MZ Twins for BMI at 9 Years and Older</li> </ul>	<p><b>TEI adjusted:</b> No</p> <p><b>Correlation between MZ twin pair differences in BMI and TEI (kcal), Spearman correlation</b>            12y: 0.07; 13y: 0.10; 14y: 0.07            Change 9-14y: 0.00</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES,</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Start of follow-up and exposure do not coincide</li> <li>77% attrition with no information on those lost to follow-up</li> <li>Weight and height self-reported</li> <li>No pre-registered data analysis plan</li> </ul> <p><b>Funding sources:</b>            Fonds Quebecois de la Recherche sur la Societe et la Culture; Fonds de la Recherche en Sante du Quebec; Social Science and Humanities Research Council of Canada; National Health Research Development Program; CIHR; Sainte-Justine Hospital Research Centre; Academy of Finland</p>



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<p><b>DuBois, 2016<sup>17</sup></b></p> <p><b>Prospective Cohort Study, Quebec Newborn Twin Study, Canada</b></p> <p>Baseline N=1324, Analytic N=304 (Attrition: 77%); Power: NR</p> <p><b>Participant characteristics: monozygotic (MZ) twin children</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean (SD): 1814.37 kcal/d (393.20)</li> <li>Sex (female): 54.6%</li> <li>Age, Mean (SD): 8.96 y (0.56)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics, Mean (SD): BMI, 16.51 (2.50)</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In MZ twins, there was not a significant association between intrapair differences in soft drink intake at age 9 and intrapair differences in BMI in subsequent years.</p>	<p><b>Exposure of interest:</b> Soft drinks</p> <p><b>Comparator:</b> Soft drinks (kcal), continuous</p> <p>Other exposures: milk, fruit juice, sugary drinks, fruit drinks</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>24-hr recall performed by registered dietitians; Represents usual intake</li> <li>At baseline (9y)</li> </ul> <p><b>Study beverage intake</b>, kcal, Mean (SD)</p> <ul style="list-style-type: none"> <li>Soft drinks: 21.27 (42.48)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (9y), 12y, 13y, 14y</li> <li>Height and weight self-reported except at baseline (measured)</li> <li>Intrapair difference (MZ twins) in BMI</li> <li>Discordant twins defined as <math>\geq 2</math> BMI units between pairs at least once at 9, 12, 13, and/or 14y</li> <li>Concordant twins defined as <math>&lt; 2</math> BMI units between pairs at all ages</li> </ul>	<p><b>Soft drink intake</b>, continuous</p> <p>Correlation between intrapair differences in intake at 9y (kcal or % energy) and intrapair differences in BMI in subsequent yrs; Spearman correlation</p> <p><b>All: kcal; % energy</b></p> <p><b>12y</b> (n=238): 0.08, NS; 0.07, NS</p> <p><b>13y</b> (n=226): 0.13, NS; 0.08, NS</p> <p><b>14y</b> (n=212): 0.04, NS; 0.01, NS</p> <p><b>Change 9-14y</b> (n=210): 0.06, NS; 0.07, NS</p> <p><b>Boys: kcal; % energy</b></p> <p><b>12y</b> (n=102): 0.04, NS; 0.03, NS</p> <p><b>13y</b> (n=96): 0.08, NS; 0.02, NS</p> <p><b>14y</b> (n=92): 0.00, NS; -0.01, NS</p> <p><b>Change 9-14y</b> (n=92): 0.01, NS; 0.01, NS</p> <p><b>Girls: kcal; % energy</b></p> <p><b>12y</b> (n=136): 0.10, NS; 0.07, NS</p> <p><b>13y</b> (n=130): 0.15, NS; 0.11, NS</p> <p><b>14y</b> (n=120): 0.14, NS; 0.08, NS</p> <p><b>Change 9-14y</b> (n=108): 0.14, NS; 0.15, NS</p> <p><b>Refer to paper and supplemental data for additional analyses on:</b></p> <ul style="list-style-type: none"> <li>Comparison of Dietary Intake (at 9 years) Among Leaner and Heavier Twins From Discordant and Concordant MZ Twin Pairs</li> <li>Comparison of Dietary Intake at 9 Years Between Discordant MZ Twins for BMI at 9 Years and Older</li> </ul>	<p><b>TEI adjusted:</b> No</p> <p><b>Correlation between MZ twin pair differences in BMI and TEI (kcal), Spearman correlation</b></p> <p>12y: 0.07; 13y: 0.10; 14y: 0.07</p> <p>Change 9-14y: 0.00</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES,</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Did not account for all key confounders</li> <li>Start of follow-up and exposure do not coincide</li> <li>77% attrition with no information on those lost to follow-up</li> <li>Weight and height self-reported</li> <li>No pre-registered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>Fonds Quebecois de la Recherche sur la Societe et la Culture; Fonds de la Recherche en Sante du Quebec; Social Science and Humanities Research Council of Canada; National Health Research Development Program; CIHR; Sainte-Justine Hospital Research Centre; Academy of Finland</p>

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<p><b>DuBois, 2016<sup>17</sup></b></p> <p><b>Prospective Cohort Study, Quebec Newborn Twin Study, Canada</b></p> <p>Baseline N=1324, Analytic N=304 (Attrition: 77%); Power: NR</p> <p><b>Participant characteristics: monozygotic (MZ) twin children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake, Mean (SD): 1814.37 kcal/d (393.20)</li> <li>• Sex (female): 54.6%</li> <li>• Age, Mean (SD): 8.96 y (0.56)</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics, Mean (SD): BMI, 16.51 (2.50)</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In MZ twins, there was not a significant association between intrapair differences in fruit drink intake at age 9 and intrapair differences in BMI in subsequent years.</p>	<p><b>Exposure of interest:</b> Fruit drinks</p> <p><b>Comparator:</b> Fruit drinks (kcal), continuous</p> <p>Other exposures: milk, fruit juice, sugary drinks, soft drinks</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• 24-hr recall performed by registered dietitians; Represents usual intake</li> <li>• At baseline (9y)</li> </ul> <p><b>Study beverage intake, kcal, Mean (SD)</b></p> <ul style="list-style-type: none"> <li>• Fruit drinks: 47.32 (64.32)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline (9y), 12y, 13y, 14y</li> <li>• Height and weight self-reported except at baseline (measured)</li> <li>• Intrapair difference (MZ twins) in BMI</li> <li>• Discordant twins defined as <math>\geq 2</math> BMI units between pairs at least once at 9, 12, 13, and/or 14y</li> <li>• Concordant twins defined as <math>&lt; 2</math> BMI units between pairs at all ages</li> </ul>	<p><b>Fruit drink intake</b>, continuous</p> <p>Correlation between intrapair differences in intake at 9y (kcal or % energy) and intrapair differences in BMI in subsequent yrs; Spearman correlation</p> <p><b>All: kcal; % energy</b></p> <p><b>12y</b> (n=238): -0.11, NS; -0.10, NS</p> <p><b>13y</b> (n=226): -0.12, NS; -0.12, NS</p> <p><b>14y</b> (n=212): -0.13, NS; -0.13, NS</p> <p><b>Change 9-14y</b> (n=210): -0.12, NS; -0.11, NS</p> <p><b>Boys: kcal; % energy</b></p> <p><b>12y</b> (n=102): -0.08, NS; -0.04, NS</p> <p><b>13y</b> (n=96): 0.07, NS; 0.07, NS</p> <p><b>14y</b> (n=92): -0.12, NS; -0.11, NS</p> <p><b>Change 9-14y</b> (n=92): -0.13, NS; -0.12, NS</p> <p><b>Girls: kcal; % energy</b></p> <p><b>12y</b> (n=136): -0.15, NS; -0.17, NS</p> <p><b>13y</b> (n=130): -0.28, NS; -0.26, NS</p> <p><b>14y</b> (n=120): -0.16, NS; -0.18, NS</p> <p><b>Change 9-14y</b> (n=108): -0.09, NS; -0.11, NS</p> <p><b>Refer to paper and supplemental data for additional analyses on:</b></p> <ul style="list-style-type: none"> <li>• Comparison of Dietary Intake (at 9 years) Among Leaner and Heavier Twins From Discordant and Concordant MZ Twin Pairs</li> <li>• Comparison of Dietary Intake at 9 Years Between Discordant MZ Twins for BMI at 9 Years and Older</li> </ul>	<p><b>TEI adjusted:</b> No</p> <p><b>Correlation between MZ twin pair differences in BMI and TEI (kcal), Spearman correlation</b></p> <p>12y: 0.07; 13y: 0.10; 14y: 0.07</p> <p>Change 9-14y: 0.00</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES,</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Start of follow-up and exposure do not coincide</li> <li>• 77% attrition with no information on those lost to follow-up</li> <li>• Weight and height self-reported</li> <li>• No pre-registered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>Fonds Quebecois de la Recherche sur la Societe et la Culture; Fonds de la Recherche en Sante du Quebec; Social Science and Humanities Research Council of Canada; National Health Research Development Program; CIHR; Sainte-Justine Hospital Research Centre; Academy of Finland</p>

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<p><b>Durao, 2015</b><sup>100</sup></p> <p><b>Prospective Cohort Study, Generation XXI birth cohort, Portugal</b></p> <p>Baseline N=821, Analytic N=589; Attrition: 28%; Power: NR</p> <p><b>Recruitment:</b> from all 5 public maternity units that cover six municipalities of the metropolitan area of Porto</p> <p><b>Participant characteristics: young children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 50%</li> <li>• Age: 25.4 (1.06) mo</li> <li>• Race/ethnicity: NR</li> <li>• SES: Maternal education 10.9 (4.27)y</li> <li>• Anthropometrics: BMIZ 0.7 (0.99)</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>Soft drink intake at age 2 and BMIZ at age 4 were not significantly associated.</p>	<p><b>Exposure of interest:</b> Soft drink intake (sweetened carbonated drinks and other sweetened drinks)</p> <p><b>Comparators:</b> Soft drink, continuous</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• FFQ answered by the primary caregiver; validated</li> <li>• At 2 and 4 years, 2- and 3-day food diaries were completed, respectively</li> <li>• At age 2y and 4y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Soft drink intake: NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 1y follow-up</li> <li>• Height: at 2y, either recumbent length (with a length measuring board) or height (using a wall Stadiometer) was measured; At 4y, height measured with wall stadiometer</li> <li>• Weight measured with digital scale</li> <li>• BMI calculated as kg/m<sup>2</sup></li> <li>• Age- and sex-specific BMI z-scores (BMIZ) according to the World Health Organization Child Growth Standards</li> </ul>	<p><b>BMIZ</b>, at 4y, and soft drink consumption at 2y: Data NR, P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, physical activity (at 4y)</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, race/ethnicity, SES, anthropometry at baseline, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Maternal age, maternal BMI, screen time (at 4y)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No information on non-completers</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b> Programa Operacional de Sau´de—Sau´de XXI; Quadro Comunita´rio de Apoio III; Administrac¸a˜o Regional de Sau´de Norte (Regional Department of Ministry of Health); Portuguese Foundation for Science and Technology; Calouste Gulbenkian Foundation</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Enes, 2013<sup>102</sup></b>  <b>Prospective Cohort Study, Brazil</b>  Baseline N=431, Follow-up N=299, Analytic N=256 (Attrition: 30.6%); Power: NR</p> <p><b>Recruitment:</b> probabilistic sample of adolescents from public schools in the city of Piracicaba, Sao Paulo, Southeastern Brazil</p> <p><b>Participant characteristics: adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d, Mean (SD): 2417.6 (332.35)</li> <li>Sex (female): 56%</li> <li>Age: 11.8 (1.35) y</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI z-score, 0.4 (1.29)</li> <li>Physical activity (h/d): 1.2 (1.07)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In a sample of Brazilian adolescents, an increase in sweetened fruit juice intake was significantly associated with a greater increase in BMI z-score over 1-year period.</p>	<p><b>Exposure of interest:</b> Change in sweetened fruit juice (natural fruit juice with added sugar) intake over 1 year</p> <p><b>Comparator:</b> Sweetened juice intake (continuous; svg/d)</p> <p>Other exposures measured: SSBs</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents usual intake over the past six months</li> <li>At baseline, 1y follow-up</li> </ul> <p><b>Study beverage intake:</b> svg/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>Sweetened fruit juice intake: 2.2 (0.77)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 1y follow-up</li> <li>Height measured to nearest mm using stadiometer attached to wall with no baseboards</li> <li>Weight measured to nearest 0.1 kg using electronic platform scale</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>BMI z-score converted from BMI using WHO growth reference for school-aged children and adolescents</li> </ul>	<p><b>Change in BMIZ over 1y</b>, Multivariate stepwise linear regression  <b>Change per svg/d increase:</b>  <b>B: 0.053, 95% CI: 0.004, 0.102 (P=0.03)</b></p>	<p><b>TEI adjusted:</b> No  <b>TEI, kcal/d, Mean (SD): Baseline, 1y 2417.6 (332.35), 2358.9 (328.48), P&lt;0.01</b></p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline</li> <li>Other factors considered: None</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES, physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Interval between study interviews, sexual maturation</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Baseline intake not adjusted for</li> <li>Attrition 31% and those who dropped out were older and had higher SSB consumption</li> <li>Reasons for exclusion and potential variation across exposure levels unclear</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  State of Sao Paulo Research Support Foundation (FAPESP)</p>

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<p><b>Enes, 2013<sup>102</sup></b>  <b>Prospective Cohort Study, Brazil</b>  Baseline N=431, Follow-up N=299, Analytic N=256 (Attrition: 30.6%); Power: NR</p> <p><b>Recruitment:</b> probabilistic sample of adolescents from public schools in the city of Piracicaba, Sao Paulo, Southeastern Brazil.</p> <p><b>Participant characteristics: adolescents</b></p> <ul style="list-style-type: none"> <li>• Total energy intake, kcal/d, Mean (SD): 2417.6 (332.35)</li> <li>• Sex (female): 56%</li> <li>• Age: 11.8 (1.35) y</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI z-score, 0.4 (1.29)</li> <li>• Physical activity (h/d): 1.2 (1.07)</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In a sample of Brazilian adolescents, SSB intake was not significantly associated with change in BMI z-score over 1-year period.</p>	<p><b>Exposure of interest:</b> SSB intake (regular soda, coffee, sweetened iced tea, noncarbonated fruit drinks)</p> <p><b>Comparator:</b> SSB intake (continuous; svg/d)</p> <p>Other exposures measured: Sweetened fruit juice</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated FFQ; represents usual intake over the past six months</li> <li>• At baseline, 1y follow-up</li> </ul> <p><b>Study beverage intake:</b> svg/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>• SSB intake: 0.7 (1.00)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 1y follow-up</li> <li>• Height measured to nearest mm using stadiometer attached to wall with no baseboards</li> <li>• Weight measured to nearest 0.1 kg using electronic platform scale</li> <li>• BMI calculated as kg/m<sup>2</sup></li> <li>• BMI z-score converted from BMI using WHO growth reference for school-aged children and adolescents</li> </ul>	<p><b>Change in BMIZ over 1y</b>, Multivariate stepwise linear regression</p> <p><b>Change per svg/d increase:</b> NS; Data NR</p>	<p><b>TEI adjusted:</b> No</p> <p><b>TEI, kcal/d, Mean (SD): Baseline, 1y</b> 2417.6 (332.35), 2358.9 (328.48), P&lt;0.01</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline</li> <li>• Other factors considered: None</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Interval between study interviews, sexual maturation</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Baseline intake not adjusted for</li> <li>• Attrition 31% and those who dropped out were older and had higher SSB consumption</li> <li>• Reasons for exclusion and potential variation across exposure levels unclear</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  State of Sao Paulo Research Support Foundation (FAPESP)</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Field, 2014</b><sup>103</sup></p> <p><b>Prospective Cohort Study, Growing Up Today Study (GUTS) II cohort, United States</b></p> <p>Baseline N=10919; Analytic N=7559; Attrition: 31%; Power: NR</p> <p><b>Recruitment:</b> recruited by sending letters to women in the Nurses' Health Study II who had children aged 9-15 years</p> <p><b>Participant characteristics: adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 55%</li> <li>Age: ~13y (Range 9-16y)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI ~20; Overweight ~20%</li> <li>Physical activity, vigorous: ~7h/w</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>Neither baseline soda intake nor change in soda intake was significantly associated with change in BMI up to 7y later. However higher sports drink intake at baseline was associated with increases in BMI scores in girls and boys. In boys, increasing the amount of sports drinks consumed over time was also associated with higher BMI scores.</p>	<p><b>Exposure of interest:</b> Soda intake; sports drink intake</p> <p><b>Comparators:</b> intake, continuous; svg/d</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Youth/Adolescent questionnaire; validated</li> <li>At baseline and 2y, 4y, 7y follow-up</li> </ul> <p><b>Study beverage intake:</b> NR</p> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline and 2y, 4y, 7y follow-up</li> <li>Weight and height self-reported</li> <li>BMI calculated as kg/m<sup>2</sup></li> </ul>	<p><b><u>Change in BMI with baseline intake and change in intake.</u></b> <math>\beta</math> (95% CI)</p> <p>[Note: change in intake was adjusted for baseline intake in these results. Analyses looking at only baseline intake or change in intake without adjusting for baseline are presented in the paper]</p> <p><b><u>GIRLS:</u></b></p> <p>Regular soda: 0.02 (-0.14, 0.19) Change in soda: 0.12 (-0.05, 0.29) <b>Sports drinks: 0.29 (0.03, 0.54)</b> Change in sports drinks: 0.05 (-0.19, 0.29)</p> <p><b><u>BOYS:</u></b></p> <p>Regular soda: 0.09 (-0.06, 0.24) Change in soda: 0.14 (-0.02, 0.30) <b>Sports drinks: 0.33 (0.09, 0.58)</b> <b>Change in sports drinks: 0.43 (0.19, 0.66)</b></p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Tanner stage of development (boys only), hours per day of television viewing, time between assessments, baseline and change values for other 2 beverages of interest</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 31% without information on non-completers</li> <li>Weight and height self-reported</li> <li>Follow-up time may have varied as participants were included if they had weight data on <math>\geq 2</math> consecutive assessment points</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>Breast Cancer Research Foundation and NIH</p>

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<p><b>French, 2012<sup>105</sup></b>  <b>Prospective Cohort Study, from RCT, United States</b></p> <p>Baseline N=NR, Analytic N= 225; Attrition: NR (overall trial attrition: ~9%); Power: among 72 adolescents, a correlation of changes between behavior and BMI z score of .60 of a standard deviation is detectable with 80% power. Among 153 adults, this detectable difference is estimated to be .38</p> <p><b>Recruitment:</b> households recruited from community libraries, worksites, schools, daycare centers, health clinics, religious institutions, park and recreation centers, grocery stores, and food co-ops</p> <p><b>Participant characteristics: households</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): Adolescents 39%; Adults 61%</li> <li>• Age: Adolescents ~15y (Range 12-17y); adults ~41y</li> <li>• Race/ethnicity: ~77% white</li> <li>• SES: Adolescents, ≤\$45K 43%; Adults ≥\$100K 43%</li> <li>• Anthropometrics: Adolescents BMIZ: ~0.71; Adults BMI ~27.2 kg/m<sup>2</sup></li> <li>• Physical activity: adolescents:~105; adults: ~85</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  SSB intake was not significantly associated with 12 month changes in BMI or BMIZ in adults or adolescents, respectively.</p>	<p><b>Exposure of interest:</b> SSBs (fruit drinks, such as cranberry cocktail, Hi-C, lemonade, or Kool-Aid; regular (non-diet) soft drinks, soda, or pop)</p> <p><b>Comparators:</b> categorical: difference between intake at 12mo and baseline, portions/wk</p> <ul style="list-style-type: none"> <li>• Decrease</li> <li>• No change/increase</li> </ul> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Modified FFQ; intake over past month; validation not clear</li> <li>• At baseline and 12mo (after 12mo intervention)</li> </ul> <p><b>Study beverage intake:</b> SSB, portions/wk</p> <ul style="list-style-type: none"> <li>• Adolescents: ~0.28</li> <li>• Adults: ~0.14</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline and 12mo</li> <li>• Height and weight measured by trained research staff</li> <li>• BMI calculated for adults</li> <li>• BMIZ calculated for adolescents</li> <li>• Weight measured using mechanical weight or beam-scale</li> <li>• Age- and sex-specific BMI z-scores (BMIZ) calculated using Lambda-Mu-Sigma method</li> <li>• Obesity (BMI&gt;30 kg/m<sup>2</sup>)</li> </ul>	<p><b>Change in BMIZ/BMI</b> per SSB change over 12mo, LSMean (SE)</p> <p><b>Adolescents (BMIZ)</b></p> <ul style="list-style-type: none"> <li>• Decrease (n= 28): 0.75 (0.08)</li> <li>• No change/increase (n=38): 0.75 (0.07)</li> </ul> <p>P=0.99</p> <p><b>Adults (BMI)</b></p> <ul style="list-style-type: none"> <li>• Decrease (n=78): 29.06 (0.18)</li> <li>• No change/increase (n=68): 29.54 (0.19)</li> </ul> <p>P=0.09</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: adult age, adult race/ethnicity, SES, anthropometry at baseline, smoking</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, physical activity</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Treatment group, household identification number, baseline SSB intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Attrition can't be determined because baseline n NR</li> <li>• Bias due to missing data can't be determined</li> <li>• Exposure data collection tool validation not clear</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH, NCI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Gopinath, 2013<sup>107</sup></b>  <b>Prospective Cohort Study, Sydney Childhood Eye Study, Australia</b>  Baseline N=2353, Analytic N=1213; Attrition: 48%; Power: NR</p> <p><b>Recruitment:</b> stratified random cluster sample of 21 high schools across Sydney</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49%</li> <li>Age: ~12y</li> <li>Race/ethnicity: ~63% Caucasian</li> <li>SES: parent with tertiary education ~53%</li> <li>Anthropometrics: BMI ~20 kg/m<sup>2</sup></li> <li>Physical activity: ~0.85 h/d</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In adolescent girls, drinking more than 1 soft drink per day compared to rarely/never drinking soft drinks was associated with greater increases in BMI, body fat %, and waist circumference 5 years later. No results were reported in boys.</p>	<p><b>Exposure of interest:</b> Frequency of soft drink (Note: cordial (a sweet flavored concentrated syrup that is mixed with water to taste) and fruit juice consumption data collected but not reported)</p> <p><b>Comparators:</b> categorical</p> <ul style="list-style-type: none"> <li>Never/rarely</li> <li>Up to 1/wk</li> <li>2-6/wk</li> <li>≥ 1/day</li> </ul> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>FFQ designed for specific use in Australian children and adolescents; data on frequency rather than amount; validated</li> <li>At baseline, 5y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Soft drinks: ≤1/wk ~48%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 5y follow-up</li> <li>Weight measured using a standard portable weighing machine</li> <li>Height was measured using a freestanding SECA height rod</li> <li>Body fat percentage (utilizing leg--leg bioimpedance analysis) were measured using a Body Composition Analyser</li> <li>WC: mid-point between the lower rib border and iliac crest measured with a measuring tape</li> <li>BMI was calculated as kg/m<sup>2</sup></li> </ul>	<p><b>GIRLS:</b>  <u>Change in BMI</u>  <b>Soft drink intake at baseline: Never/rarely (3.20) vs ≥ 1/day (1.96) P=0.01</b>  Other comparisons NR  P-trend= NS</p> <p><u>Change in Body fat %</u>  <b>Soft drink intake at baseline: Never/rarely (-0.66) vs ≥ 1/day (3.79) P-trend=0.01</b>  Other comparisons NR</p> <p><u>Change in WC</u>  <b>Soft drink intake at baseline: Never/rarely (6.46) vs ≥ 1/day (10.00), P=0.004</b>  Other comparisons NR  P-trend= NS</p> <p><b>BOYS:</b>  <u>Change in BMI:</u> NR  <u>Change in Body fat %:</u> NR  <u>Change in WC:</u> NR</p> <p>Frequency of cordial (a sweet flavored concentrated syrup that is mixed with water to taste), and fruit juice consumption: NR</p>	<p>TEI adjusted: Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: N/A</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>High attrition rate</li> <li>Exposure not well defined (likely did not but may have included LNCSBs)</li> <li>Reported SSB analyses only used baseline exposure measure</li> <li>No preregistered data analysis plan; did not report complete set of results in girls; did not report results for boys; did not report results per consumption of cordials and juice</li> </ul> <p><b>Funding sources:</b>  Australian National Health &amp; Medical Research Council; the Westmead Millennium Institute, University of Sydney; the Vision Co-operative Research Centre, University of New South Wales, Sydney; and the National Heart Foundation of Australia</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Guerrero, 2016<sup>70</sup></b>  <b>Prospective Cohort Study, Early Childhood Longitudinal Study-Birth Cohort (ECLS-B), United States</b>  Baseline N= NR, Analytic N= 15418; Attrition: NR; Power: NR</p> <p><b>Recruitment:</b> non-probability birth sample was drawn in 2001 for the ECLS-B by the National Center for Education Statistics</p> <p><b>Participant characteristics: young children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 49%</li> <li>• Age: 53 (4.1) mo</li> <li>• Race/ethnicity: 43% White, 16% Black, 11% Asian, 10% Other, 20% Hispanic, 9% Spanish speaking; Maternal education: 21% High school, 27% College, 31% ≥Bachelor</li> <li>• SES: 79% lived in 2-parent households; ~25% below fed poverty level</li> <li>• Anthropometrics: BMI ~16.5; ~33% ovwt or ob</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Soda consumption was associated with increased BMI trajectory for the full sample of children as well as for Black and Hispanic-Spanish speaking children, but not for White, Asian, or Hispanic-English speaking children.</p>	<p><b>Exposure of interest:</b> Soda intake</p> <p><b>Comparator:</b> Soda intake, categorical:</p> <ul style="list-style-type: none"> <li>• Any intake in the last 7d</li> <li>• No intake in the last 7d</li> </ul> <p>Other exposure measures: 100% fruit juice</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Parental interview: "Was soda consumed in past 7d? Yes/No"</li> <li>• At 48, 60, and 72mo of age</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Any soda last week (age 48mo): ~71%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At 48, 60, and 72mo of age</li> <li>• Height and weight obtained by trained researchers using standardized procedures and equipment</li> <li>• Age- and sex-specific BMI percentiles and z-scores (BMIZ) calculated using 2000 CDC growth charts</li> <li>• Overweight: BMI 85<sup>th</sup>-&lt;95<sup>th</sup>%</li> <li>• Obesity: BMI ≥95%</li> </ul>	<p><b>BMI trajectory</b>, Hierarchical linear modeling, <math>\beta</math> (SE)  <b>No soda (ref) vs Soda within 7d: 0.138 (0.037), P&lt;0.05</b></p> <p><i>By race:</i> No soda (ref) vs soda within 7d; <math>\beta</math> (SE)</p> <ul style="list-style-type: none"> <li>• White: 0.087 (0.054), NS</li> <li>• <b>Black: 0.288 (0.107), P&lt;0.01</b></li> <li>• Asian: 0.065 (0.100), NS</li> <li>• Hispanic-English: 0.027 (0.139), NS</li> <li>• <b>Hispanic-Spanish: 0.234 (0.115), P&lt;0.05</b></li> </ul>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Birth weight, mother's acculturation, breastfeeding during infancy, soda intake, fast food consumption, daily servings of fruits and vegetables</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Baseline, analytic sample sizes and attrition not clear</li> <li>• Exposure data collection tool not validated</li> <li>• Does not account for amount of exposure (just y/n within 7d)</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  HHS; University of California's Institute of Human Development; McCormick Foundation</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Hasnain, 2014<sup>27</sup></b>  <b>Prospective Cohort Study, Framingham Children's Study, United States</b>            Baseline N=106, Analytic N=98 (Attrition: 8%); Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~1724 kcal/d</li> <li>Sex (female): 55.1%</li> <li>Age: 3-5y</li> <li>Race/ethnicity: 100% non-Hispanic white</li> <li>SES: Maternal education &gt;college, ~34%; 100% 2-parent household</li> <li>Anthropometrics: BMI, Mean~16.1</li> <li>Physical activity: Mean~10.7 Caltrac counts/hr</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            Sugar sweetened beverage intake from 3-9y was not significantly associated with body fat %, BMI, sum of skinfolds, or waist circumference at 15-17y.</p>	<p><b>Exposure of interest:</b> SSBs (sweetened carbonated beverages, sweetened noncarbonated beverages, sweetened tea or coffee, part-juice beverages)</p> <p><b>Comparators:</b> SSB intake (categorical; tertiles)</p> <ul style="list-style-type: none"> <li>T1 (Mean=2.8 oz/d, SD=1.2)</li> <li>T2 (Mean=5.8 oz/d, SD=0.9)</li> <li>T3 (Mean=10.7 oz/d, SD=2.6)</li> </ul> <p>Other exposures: milk, fruit and vegetable juice, unsweetened/diet beverages</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Up to 4 sets of 3-d diet records annually completed by parents; Represents usual intake</li> <li>At baseline (3-5y), annually for 12y (age 15-17y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSBs, Median (5<sup>th</sup>, 95<sup>th</sup> percentile): 4.5 oz/d (0.0, 14.1)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>End of follow-up (15-17y)</li> <li>Weight, height, waist circumference measured by study personnel</li> <li>Four skinfolds (triceps, subscapular, suprailiac, abdominal) measured in duplicate following standard protocol</li> <li>Percent body fat measured with DXA scan</li> </ul>	<p><b><u>Effects of intake (by tertiles) at ages 3-9y on outcomes at end of follow-up (ages 15-17y): linear regression</u></b>  <b>Body fat %</b>, Data NR, P=0.9296  <b>BMI</b>, kg/m<sup>2</sup>: Data NR, P=0.4204  <b>Sum of 4 skinfolds</b>, mm: Data NR, P=0.9790  <b>WC<sub>1</sub></b> cm: Data NR, P=0.3494</p> <p><b><u>Effects of intake (by tertiles) on sum of skinfolds over time; mixed model</u></b>  <b>Sum of 4 skinfolds</b>            T1 vs T2: Data NR, P=0.1121            T1 vs T3: Data NR, P=0.8807            T2 vs T3: Data NR, P=0.0737</p>	<p><b>TEI adjusted:</b> Evaluated but not independent predictor so removed from model</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Percent of calories from fat, mean TV and video time, other beverages consumed, maternal education, maternal BMI</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Validation of 3-d diet records not indicated</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>            NHLBI; National Dairy Council</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Hooley, 2012<sup>109</sup></b>  <b>Prospective Cohort Study, Longitudinal Study of Australian Children (LSAC), Australia</b>  Baseline N=NR, Analytic N= 4149; Attrition: NR; Power: NR</p> <p><b>Recruitment:</b> a two-stage clustered sampling design stratified by both a state and a city/'rest of state' division and clustered by postcode within each stratum, so that about 1 out of 10 Australian postcodes were included in the study</p> <p><b>Participant characteristics: young children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 48%</li> <li>• Age: ~4.8y</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMIZ 0.55; 21% overweight/obese</li> <li>• Physical activity: NR</li> <li>• Smoking: smoker in house ~13%</li> </ul> <p><b>Summary of findings:</b>  Increased high sugary drink consumption was associated with higher relative risk of being overweight/obese 2y later.</p>	<p><b>Exposure of interest:</b> High-sugar drinks (HSD; fruit juice, soft drink or cordial; not diet)</p> <p><b>Comparators:</b> continuous</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• "Time use diaries": Parent-reported frequency of consumption in the 24 h prior to the survey; not validated</li> <li>• At baseline, 2y, 4y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• High-sugar drinks at baseline: 1.7 times/d</li> <li>• High-sugar drinks at 2y follow up: 1.4 times/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 2y, 4y follow-up</li> <li>• Weight and height measured</li> <li>• Waist circumference (WC) measured horizontally around naval with non-stretch tape</li> <li>• Classified as underweight, normal weight, overweight or obese according to the International Obesity Task Force age- and sex-specific criteria for BMI</li> </ul>	<p><b>Weight status at 4y follow-up,</b> association with sweet drink intake at 2y follow-up (<i>not baseline</i>): RRR (LSE) Thin: 1.07 (0.10), P=0.43  Normal: ref  <b>Overweight/obese: 1.10 (0.05), P=0.02</b></p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, smoking</li> <li>• Other factors considered: alcohol during pregnancy</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: anthropometry at baseline, physical activity</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Breastfed, frequency of tooth brushing, maternal BMI, maternal age, maternal smoking during pregnancy, number of smokers in household</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Baseline n, attrition NR</li> <li>• Exposure data collection tool not validated</li> <li>• Exposure data based on previous day only, may not reflect usual intake</li> <li>• No information on missing data/non-completers</li> <li>• No preregistered data analysis plan: associations between baseline and follow-up NR</li> <li>• Funding source NR</li> </ul> <p><b>Funding sources:</b>  NR</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Jensen, 2013</b><sup>110</sup></p> <p><b>Prospective Cohort Study, Be Active Eat Well (BAEW) and It's Your Move! (IYM), Australia</b></p> <p>Baseline N=2371, Analytic N=1465; Attrition: 38%; Power: NR</p> <p><b>Recruitment:</b> BAEW: a random sample of primary schools selected from the Barwon–South Western Region of Victoria</p> <p><b>Participant characteristics: children, adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): BAEW: 50%; IYM: 53%</li> <li>Age: BAEW: ~8y; IYM: ~14.6y</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BAEW: BMI 17.6; BMIZ 0.8; IYM: BMI 21.6; BMIZ 0.5</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>There was no significant association between sweet drink intake and BMIZ 2 years later. No significant association was found between change in sweet drink intake over 2y and BMIZ in adolescents or low SES children; however, increased intake over 2y was associated with increased BMIZ in high SES children.</p>	<p><b>Exposure of interest:</b> Sweet drink consumption (non-diet soft drinks, fruit juice (including 100% juice), and cordials)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Continuous (per 100 mL)</li> <li>Categorical, based on change from baseline to follow-up <ul style="list-style-type: none"> <li>No change (ref)</li> <li>Intake decreased</li> <li>Intake increased</li> </ul> </li> </ul> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Questionnaire (different for each cohort); not validated</li> <li>At baseline, ~2y follow-up</li> </ul> <p><b>Study beverage intake at baseline:</b> Median</p> <ul style="list-style-type: none"> <li>Children (BAEW): 375mL</li> <li>Adolescents (IYM): 500mL</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, ~2y follow-up</li> <li>Weight and height measured by trained researchers</li> <li>BMI calculated</li> <li>BMIZ calculated using WHO Growth Standard and Growth Reference</li> </ul>	<p><b><u>BMIZ at 2y follow-up, with sweet drink intake at baseline:</u></b> linear regression, <math>\beta</math> (95%CI)</p> <p><b>BAEW:</b> 0.005 (-0.003, 0.012), P=0.18</p> <p><b>IYM:</b> 0.004 (-0.002, 0.01), P=0.15</p> <p><b><u>BMIZ at 2y follow-up, with change in sweet drink intake:</u></b> <math>\beta</math> (95%CI)</p> <p><b>BAEW-low SES:</b></p> <ul style="list-style-type: none"> <li>No change: (ref)</li> <li>Intake decreased: -0.013 (-0.110, 0.084), P=0.78</li> <li>Intake increased: -0.048 (-0.181, 0.085), P=0.45</li> </ul> <p><b>BAEW-High SES:</b></p> <ul style="list-style-type: none"> <li>No change: (ref)</li> <li>Intake decreased: 0.096 (-0.123, 0.314), P=0.36</li> <li><b>Intake increased: 0.128 (0.003, 0.253), P=0.05</b></li> </ul> <p>[Note: Children from lower and higher SES families had similar BMI z-scores at T1, but children from higher SES families had a lower intake of sweet drinks at T1 than children from lower SES families (median lower SES: 500 mL, median higher SES: 250 mL, P &lt; 0.0001).]</p> <p><b>IYM:</b></p> <ul style="list-style-type: none"> <li>No change: (ref)</li> <li>Intake decreased: -0.078 (-0.188, 0.033), P=0.14</li> <li>Intake increased: -0.027 (-0.123, 0.070), P=0.52</li> </ul>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> School cluster, duration between measurements</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure data collection tool not validated</li> <li>Exposure includes 100% juice and only assessed previous 24hr; 'usual intake' was assessed but only analyzed in supplemental material</li> <li>No preregistered data analysis plan; did not fully report results for sweet drink types</li> </ul> <p><b>Funding sources:</b></p> <p>IYM: Victorian Department of Health, National Health and Medical Research Council, Health Research Council (New Zealand), Wellcome Trust (UK), AusAID</p> <p>BAEW: Commonwealth Department of Health and Ageing, Victorian Department of Human Services, Victorian Health Promotion Foundation (VicHealth)</p>

**Jensen, 2013<sup>111</sup>**

**Prospective Cohort Study,  
Copenhagen School Child  
Intervention Study  
(CoSCIS), Denmark**

Baseline N=1024, Analytic N=269;  
Overall trial attrition over ~6y: 50%;  
Power: Minimum association level was  
determined for recruited (ie, after  
enrollment) sample size at 80% and  
significance level of 5%

**Recruitment:** all children entering a  
public school in two suburbs of  
Copenhagen, Denmark in 2001, were  
invited to participate

**Participant characteristics: children**

- Total energy intake: ~8.3 MJ/d
- Sex (female): 51%
- Age: ~6.7y
- Race/ethnicity: NR
- SES: Maternal Education:  
Elementary: 28%; High school/short  
ed: 38%; College: 35%
- Anthropometrics: BMI ~16;  
Ovwt/ob: 13%
- Physical activity: 731 cpm
- Smoking: NR

**Summary of findings:**

Intake of sweet drinks (as well as  
subgroups SSBs and soft drinks) was not  
significantly associated with change in  
BMI or change in skinfold thickness in  
children.

**Exposure of interest:** Sweet drinks: soft  
drink, squash, fruit juice, chocolate milk  
and drinkable yoghurt; SSB (subgroup):  
soft drink and squash; Artificially  
sweetened (i.e. light or non-caloric)  
beverages were not included (100 mL =  
100g = 3.38 US fl oz)

**Comparators:** continuous

**Exposure assessment method and timing:**

- 7d pre-printed food record completed  
by parents; not validated
- At baseline (6yo), 3y follow-up (9yo)

**Study beverage intake:** Median g/d

- Sweet drinks: 383
- Soft drink: 114
- Squash: 143
- Fruit juice: 26

**Outcome assessment methods/timing:**

- At baseline (6yo), 3y and 7y follow-up  
(9yo, 13yo)
- Weight and height measured by  
trained researchers
- Skin-fold thicknesses (mm) measured  
with Harpenden calipers at four points  
on the non-dominant side of the body:  
(i) triceps; (ii) biceps; (iii) subscapular  
and (iv) supra iliac
- BMI calculated

**Change in BMI**, linear regression,  $\beta$   
(95% CI)

**Intake at 6y, BMI change 6-9y** (n=366):  
Sweet drinks: -0.0140 (-0.0628, 0.0349),  
P=0.55

SSBs: -0.0051 (-0.0591, 0.0489), P=0.84  
Soft drinks: -0.0338 (-0.1299, 0.0623),  
P=0.47

**Intake at 6y, BMI change 6-13y**

(n=286):  
Sweet drinks: -0.0492 (-0.1228, 0.0244),  
P=0.18

SSBs: -0.0592 (-0.1453, 0.0270), P=0.17  
Soft drinks: -0.0353 (-0.2178, 0.1473),  
P=0.69

**Intake at 9y, BMI change 9-13y**

(n=269):  
Sweet drinks: 0.0357 (-0.0171, 0.0884),  
P=0.17

SSBs: 0.0078 (-0.0976, 0.1131), P=0.88  
Soft drinks: 0.1090 (-0.1261, 0.3442),  
P=0.34

**Change in intake 6-9y, BMI change 9-  
13y** (n=235):

Sweet drinks: 0.0359 (-0.0391, 0.1109),  
P=0.33  
SSBs: 0.0260 (-0.0747, 0.1266), P=0.59  
Soft drinks: 0.1045 (-0.1292, 0.3382),  
P=0.36

**Change in Sum 4skinfolds**,  $\beta$  (95% CI)  
**Intake at 6y,  $\Sigma$ 4SF change 6-9y**

(n=366):  
Sweet drinks: -0.0030 (-0.0129, 0.0068),  
P=0.53

SSBs: -0.0034 (-0.0138, 0.0071), P=0.50  
Soft drinks: -0.0069 (-0.0294, 0.0157),  
P=0.53

**Intake at 6y,  $\Sigma$ 4SF change 6-13y**

(n=286):  
Sweet drinks: -0.0024 (-0.0136, 0.0088),  
P=0.65

SSBs: -0.0043 (-0.0187, 0.0101), P=0.54  
Soft drinks: -0.0040 (-0.0381, 0.0301),  
P=0.81

**Intake at 9y,  $\Sigma$ 4SF change 9-13y**

(n=269):

**TEI adjusted:** Yes & No

TEI-adjusted data available in paper for  
some supplemental analyses only. Overall,  
the relationship between overall sweet  
drink at 9y and  $\Sigma$ 4SF change 9-13y was  
the only impacted relationship

**Confounders accounted for:**

- Key confounders: sex, SES,  
anthropometry at baseline
- Other factors considered: n/a

**Confounders NOT accounted for:**

- Key confounders: age, race/ethnicity,  
physical activity, smoking
- Other factors considered: total energy  
intake, timing, temporal use, sugar,  
protein, fiber, energy density,  
medications, supplements, alcohol

**Additional model adjustments:** School,  
intervention/comparison group, pubertal  
status

**Limitations:**

- Not all key confounders accounted for
- High attrition without information on  
non-completers
- Exposure data collection tool not  
validated
- No preregistered data analysis plan;  
results from all analyses NR

**Funding sources:**

Tryg Foundation; Centre for Intervention  
Research in Health Promotion and Disease  
Prevention; The Danish Heart Foundation;  
'Familien Hede Nielsen' Foundation;  
University of Southern Denmark

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
		<p>Sweet drinks: 0.0140 (-0.0009, 0.0290), P=0.06</p> <p>SSBs: 0.0176 (-0.0078, 0.0430), P=0.16</p> <p>Soft drinks:</p> <ul style="list-style-type: none"> <li>▪ Comparison grp: -0.0441 (-0.0971, 0.0090), P=0.09</li> <li>▪ <b>Intervention grp: 0.0871 (0.0480, 0.1263), P=0.001</b></li> </ul> <p><b>Change in intake 6-9y, Σ4SF change 9-13y (n=235):</b></p> <p>Sweet drinks: 0.0162 (-0.0020, 0.0343), P=0.08</p> <p>SSBs: 0.0206 (-0.0075, 0.0486), P=0.14</p> <p>Soft drinks: 0.0414 (-0.0097, 0.0924), P=0.11</p>	

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Johnson, 2012</b><sup>112</sup>  <b>Prospective Cohort Study</b>  <b>(Longitudinal analyses from a cluster NRCT), Be Active Eat Well (BAEW), Australia</b>  Baseline N=2909, Analytic N=1812;  Attrition for overall trial: 16%; Power: NR</p> <p><b>Recruitment:</b> from preschools and primary schools from the Barwon South-West region of Victoria</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): ~52%</li> <li>• Age: ~8y (Range 4-12y)</li> <li>• Race/ethnicity: NR</li> <li>• SES: mother didn't complete HS ~45%</li> <li>• Anthropometrics: BMI ~17.8; BMIZ ~63</li> <li>• Physical activity: outside play ~1.25h/d</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  An increase in sweet drink consumption over ~2.5y is associated with an increase in BMIZ over the same period in children.</p>	<p><b>Exposure of interest:</b> Sweet drinks (1 Serve=250 ml of soft drink, <i>100% fruit juice</i>, diluted fruit juices or cordials, including energy containing flavored mineral water and sports drinks)</p> <p><b>Comparators:</b> continuous</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Computer-assisted telephone interview from parents/guardians; from previous day intake; not validated</li> <li>• At baseline, ~2.5y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Sweet drink (serves): ~2</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, ~2.5y follow-up</li> <li>• Weight and height measured by trained researchers</li> <li>• BMIZ derived using the zanthro function in Stata against the US CDC 2000 reference population</li> </ul>	<p><b>Change in BMIZ</b>, by change in Sweet drink consumption, multilevel model, <math>\beta</math> (95% CI)  <b>0.015 (0.00, 0.03), P=0.02</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, SES, anthropometry at baseline</li> <li>• Other factors considered: n/a</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Intervention group</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No information on non-completers</li> <li>• Exposure data collection tool not validated and only represents previous day, not habitual intake</li> <li>• Exposure includes 100% fruit juice</li> <li>• Follow-up time varied substantially across participants (original intervention vs. control group)</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Commonwealth Department of Health and Ageing; Victorian Department of Human Services and the Victorian Health Promotion Foundation (VicHealth); VicHealth Public Health Research Fellowship and the Jack Brockhoff Child Health and Wellbeing Program</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Laska, 2012</b><sup>116</sup></p> <p><b>Prospective Cohort Study, Identifying Determinants of Eating and Activity (IDEA) and Etiology of Childhood Obesity (ECHO), United States</b></p> <p>Baseline N=723, Analytic N=535 (Attrition: 26%); Power: NR</p> <p><b>Recruitment:</b> existing cohort, application list from State department of motor vehicles, convenience sample within community, and from membership base of Health Partners (large HMO in Minnesota)</p> <p><b>Participant characteristics: adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake: 1982 kcal/d</li> <li>Sex (female): 51%</li> <li>Age: 14.6y</li> <li>Race/ethnicity: ~85% White</li> <li>SES: ~75% Parent college graduate; ~11% Eligible for free/reduced lunch</li> <li>Anthropometrics: BMI 22.0 kg/m<sup>2</sup></li> <li>Physical activity: 310 min/d</li> <li>Smoking: NR</li> </ul> <p>Note: Characteristics are stratified by sex in the paper</p> <p><b>Summary of findings:</b></p> <p>In adolescents, greater SSB intake was significantly associated with increases in BMI and percent body fat at 2y follow-up in males. SSB intake was not related to either outcome in females. After adjusting for multiple comparisons, the relationship with SSB intake &amp; %BF in males when adjusting for TEI was the only finding that remained significant.</p>	<p><b>Exposure of interest:</b> SSB intake (sweetened soft drinks, fruit drinks, tea, coffee, and/or coffee substitutes)</p> <p><b>Comparator:</b> SSB intake (continuous; svg/d)</p> <p>Other exposure measures: Diet soda</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Three 24hr recalls (self-report via telephone); represents 2 weekdays and 1 weekend day</li> <li>At baseline, 2y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Males: SSB intake at baseline: 1.02 svg/d; 2y follow up: 1.03 svg/d</li> <li>Females: SSB intake at baseline: 0.70 svg/d; 2y follow up: 0.65 svg/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 2y follow-up</li> <li>Height measured without shoes using Shorr Height Board to nearest 0.1 cm</li> <li>Weight (to nearest 0.1 kg) and percent body fat (%BF) assessed using digital bioelectrical impedance scale</li> </ul>	<p><b>MALES</b></p> <p><b>BMI</b>, kg/m<sup>2</sup>, Change per svg/d increase of SSB, Random coefficients model/mixed model, <math>\beta</math> (SE)</p> <p><b>TEI unadj: 0.25 (0.10), P=0.012</b></p> <p><b>TEI adj: 0.27 (0.10), P=0.008</b></p> <p>(Note: these findings with BMI were significant at <math>p&lt;0.05</math> but was not significant at the p-value cutoff used to adjust for multiple comparisons (<math>p&lt;0.003</math>))</p> <p><b>%BF</b>, Change per svg/d increase of SSB, Linear regression, <math>\beta</math> (SE)</p> <p><b>TEI unadj: 0.51 (0.22), P=0.018</b></p> <p><b>TEI adj: 0.73 (0.21), P=0.001</b></p> <p>(Note: the (unadjusted for TEI) finding with %BF was significant at <math>p&lt;0.05</math> but was not significant at the p-value cutoff used to adjust for multiple comparisons (<math>p&lt;0.003</math>)).</p> <p><b>FEMALES</b></p> <p><b>BMI</b>, kg/m<sup>2</sup>, Change per svg/d increase of SSB, Linear regression, <math>\beta</math> (SE)</p> <p>TEI unadj: -0.09 (0.16), P=0.585</p> <p>TEI adj: -0.05 (0.17), P=0.746</p> <p><b>%BF</b>, Change per svg/d increase of SSB, Linear regression, <math>\beta</math> (SE)</p> <p>TEI unadj: -0.06 (0.33), P=0.861</p> <p>TEI adj: 0.04 (0.35), P=0.908</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b></p> <p>Puberty, study (ECHO vs. IDEA)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 26% without information on non-completers</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>NCI; NHLBI</p>



Lee, 2015<sup>117</sup>

**Prospective Cohort Study, National Lung, Heart and Blood Institute's Growth and Health Study (NGHS), United States**

Baseline N=2021, Analytic N=Visit 2-3: 1,597, Visit 3-4: 1415, Visit 4-5: 1304, Visit 7-8: 840 (Overall trial attrition: ~12%); Power: NR

**Recruitment:** by three clinical centers (Berkley, CA; Cincinnati, OH; Rockville, MD) that recruited from public and parochial schools

**Participant characteristics: girls**

- Total energy intake: 1899 (650) kcal/d
- Sex (female): 100%
- Age: 11.0 (0.57) y
- Race/ethnicity: 51% White, 49% Black
- SES: Parent education: ≤High school 24%, 1-3yr Post High School 38%, College graduate 39%
- Anthropometrics: 67% Normal weight, 15% Overweight, 14% Obese
- Physical activity: 474 (438) – units unclear
- Smoking: NR

**Summary of findings:**

In girls, before and after adjusting for total energy intake, each additional teaspoon of added liquid sugar intake was significantly associated with an increase in waist circumference over each 1yr increment from ages 11-17y. Each additional teaspoon of added liquid sugar intake was also significantly associated with an increase in BMIZ, but this was not maintained after adjustment for total energy.

**Exposure of interest:** Liquid added sugar intake (sum of fructose, glucose, and sucrose added to soft drinks, energy drinks, fruit juices, sweetened milks, and sweetened coffees and teas); 1 tsp = 4g

**Comparator:** Liquid added sugar intake (continuous; tsp/d)

Other exposure measures: none

**Exposure assessment method and timing:**

- 3-d food record; represents dietary intake on two weekdays and one weekend day
- At Visits 1-5, 7, 8, and 10\*

**Study beverage intake:** tsp/d, Mean (SD)

- Liquid added sugar intake: 9.1 (6.8)

**Outcome assessment methods/timing:**

- Annually for 10yrs (Visits 1-10\*)
- Height and weight measured twice by research staff in accordance with standard protocols
- BMI calculated as kg/m<sup>2</sup>
- Age- and sex-specific BMI z-scores (BMIZ) determined using 2000 CDC growth charts
- Weight status: Normal (BMIZ<85<sup>th</sup>%), Overweight/Obese (BMIZ≥85<sup>th</sup>%)
- Waist circumference (WC) measured following breath expiration at all visits except Visit 1

\*Note: To examine the association between simultaneous change in intake and change in adiposity, observations were selected in which 1-year change could be calculated. Four pairs of observations were available for this analysis: change between visit pairs 2 and 3, 3 and 4, 4 and 5, and 7 and 8.

Note: To examine the association between simultaneous change in intake and change in adiposity, observations were selected in which 1-year change could be calculated.

**1yr Δ in BMIZ**, Change per 1 tsp increase in liquid sugar, Linear regression, β (95% CI)

**TEI unadj: 0.002 (0.001, 0.003), P=0.003**

TEI adj: 0.001 (0.000, 0.002), P=0.10

**1yr Δ in WC**, mm, Change per 1 tsp increase in liquid sugar, Linear regression, β (95% CI)

*Normal weight*

**TEI unadj: 0.235 (0.108, 0.361), P=0.0003**

**TEI adj: 0.164 (0.026, 0.303), P=0.02**

*Overweight/obese*

**TEI unadj: 0.280 (0.091, 0.468), P=0.004**

**TEI adj: 0.207 (0.009, 0.404), P=0.04**

**TEI adjusted:** Yes and No

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity
- Other factors considered: total energy intake, sugar, fiber

**Confounders NOT accounted for:**

- Key confounders: smoking
- Other factors considered: timing, temporal use, protein, energy density, medications, supplements, alcohol

**Additional model adjustments:**

Puberty stage, dieting status, percentage of energy from fat or other carbohydrates

**Limitations:**

- Not all key confounders accounted for
- No preregistered data analysis plan

**Funding source:**

Children's Healthcare of Atlanta

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Macintyre, 2018</b><sup>119</sup>  <b>Prospective Cohort Study, Growing Up in Scotland (GUS), Scotland</b>  Baseline N=3196, Analytic N=2332  (Attrition: 27%); Power: NR</p> <p><b>Recruitment:</b> random sample of aggregated Data Zones, stratified by Local Authority Area and by Scottish Index of Multiple Deprivation</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49%</li> <li>Age: 4-5y</li> <li>Race/ethnicity: NR</li> <li>SES: Maternal education: 30% Standard grades/intermediate vocational; 33% Higher grades/upper vocational; 28% degree level academic/vocational qualifications</li> <li>Anthropometrics: BMI: 74% Healthy weight; 16% Overweight; 11% Obese</li> <li>Physical activity: 64% Met physical activity guidelines (420 min/wk)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, daily SSB consumption at age 4-5y was significantly related to higher BMI at age 7-8y. Consuming SSBs 1-6 times/wk at 4-5y was also significantly associated with risk of obesity at 7-8y; however, this did not follow a linear pattern and was only significant for the middle consumption category. There was no significant association between SSB intake at 4-5y and risk of overweight at 7-8y.</p>	<p><b>Exposure of interest:</b> SSB intake (soft drinks and diluted juice; not including diet or sugar-free drinks, fresh fruit juice, or water)</p> <p><b>Comparators:</b> SSB intake (categorical):</p> <ul style="list-style-type: none"> <li>Never or &lt;1/wk (ref)</li> <li>1-6 times/wk</li> <li>≥1/d</li> </ul> <p>Other exposure measures: artificially sweetened beverages</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Parent interview using single question on frequency of intake</li> <li>At Sweep 5: (age 4-5y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSB intake: 44%, Never or &lt;1/wk; 15%, 1-6/wk; 41%, ≥1/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At Sweep 4: (age 3-4y), and at ~3y follow-up (Sweep 7: age 7-8y)</li> <li>Height and weight measured on non-carpeted surface by GUS project team following a protocol</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>BMI classification defined according to British 1990 growth reference curves (Overweight: 85<sup>th</sup>% cutoff, Obesity: 95<sup>th</sup>% cutoff)</li> </ul>	<p><b>Overweight including Obese at 7-8y,</b> Logistic regression, OR (95% CI)  &lt;1/wk (ref) vs  1-6 times/wk: 0.94 (0.68, 1.30), P=0.69  ≥1/d: 1.18 (0.92, 1.52), P=0.19</p> <p><b>Obesity at 7-8y,</b> Logistic regression, OR (95% CI)  &lt;1/wk (ref) vs  <b>1-6 times/wk: 1.65 (1.12, 2.44), P=0.01</b>  ≥1/d: 1.19 (0.85, 1.65), P=0.30</p> <p><b>BMI,</b> kg/m<sup>2</sup>, Linear regression, β (95% CI)  &lt;1/wk (ref) vs  1-6 times/wk: 0.06 (-0.17, 0.29), P=0.59  <b>≥1/d: 0.19 (0.01, 0.37), P=0.04</b></p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Maternal age; mother's BMI; television viewing on weekdays; consumption of breakfast, fruit and vegetables, milk, water, sweets/crisps, and processed meals</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 27% without information on non-completers</li> <li>Exposure data collection tool not validated</li> <li>Exposure data only measured at baseline</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Medical Research Council; Chief Scientist Office of the Scottish Government Directorates</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Marshall, 2018<sup>2</sup></b>  <b>Prospective Cohort Study, Iowa Fluoride and Iowa Bone Development Studies, United States</b>  Baseline N=717 Analytic N=571 (Attrition: 20.4%); Power: NR</p> <p><b>Recruitment:</b> at birth</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: at 2-4.7y, Median~1360 kcal/d</li> <li>Sex (female): 51%</li> <li>Age: Range=2-4.7y</li> <li>Race/ethnicity: Non-Hispanic white 94%</li> <li>SES: Mother had 4y college degree 45%, Household annual income ≥\$60,000 19%</li> <li>Anthropometrics: Weight, Mean~20.0 kg; Height, Mean~111.4 cm</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, when controlling for energy intake, SSB intake was not significantly associated with changes in height.</p>	<p><b>Exposure of interest:</b> SSB intake</p> <p><b>Comparator:</b> SSB intake (continuous; 8 oz/d)</p> <p>Other exposure measures: milk, juice, water/other sugar-free beverages</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated beverage frequency questionnaire; represents previous week's beverage intakes</li> <li>At 3- to 6-mo intervals: 2-4.7, 5-8.5, 9-10.5, 11-12.5, 13-14.5, and 15-17y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSB intake at 2-4.7y: Median ~2.7oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At ages 5, 9, 11, 13, 15, 17y</li> <li>Height measured without shoes using stadiometer during clinic visits</li> </ul>	<p><b>Height</b>, cm, <b>Change per 8 oz/d increase</b>; Linear regression:  B: 0.15, 95% CI: -0.06, 0.36, P=0.16</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake, protein</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No information on missing data</li> <li>Registry does not contain data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>  NIH; The Roy J. Carver Charitable Trust; Delta Dental of Iowa Foundation</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Marshall, 2019<sup>41</sup></b>  <b>Prospective Cohort Study, Iowa Fluoride and Iowa Bone Development Studies, United States</b>  Baseline N=720 Analytic N=623  (Attrition: 13.5%); Power: NR</p> <p><b>Recruitment:</b> at birth</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: at 2-4.7y, Median~1360 kcal/d</li> <li>• Sex (female): 51%</li> <li>• Age: Range=2-4.7y</li> <li>• Race/ethnicity: Non-Hispanic white 94%</li> <li>• SES: Mother had 4y college degree 45%; Household annual income ≥\$60,000 19%; Low 25%, Middle 38%, High 38%</li> <li>• Anthropometrics: BMI, Mean~16.0 kg/m<sup>2</sup>; BMIZ, Mean~0.31</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, when controlling for energy intake, SSB intake was significantly associated with increases in BMIZ.</p>	<p><b>Exposure of interest:</b> SSB intake</p> <p><b>Comparator:</b> SSB intake (continuous; 8 oz/d)</p> <p>Other exposure measures: milk, juice, water/other sugar-free beverages</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated beverage frequency questionnaire; represents previous week's beverage intakes</li> <li>• At 3- to 6-mo intervals: 2-4.7, 5-8.5, 9-10.5, 11-12.5, 13-14.5, and 15-17y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• SSB intake at 2-4.7y: Median~2.65 oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At ages 5, 9, 11, 13, 15, 17y</li> <li>• Height measured without shoes using stadiometer during clinic visits</li> <li>• Weight was measured at clinic visit using a standard physician's scale</li> <li>• BMIs were calculated from weight and height measures (kg/m<sup>2</sup>)</li> <li>• Age- and sex-specific BMI z-scores (BMIZ) calculated 2000 CDC growth charts</li> </ul>	<p><b>BMIZ, Change per 8 oz/d increase in milk, Linear regression:</b>  <b>B: 0.050, 95% CI: 0.022, 0.079, P=0.001</b></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, SES</li> <li>• Other factors considered: total energy intake, protein</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Other beverage intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No information on missing data</li> <li>• Registry does not contain data analysis plan</li> <li>• Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>  NIH; The Roy J. Carver Charitable Trust; Delta Dental of Iowa Foundation</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Millar, 2014</b><sup>121</sup></p> <p><b>Prospective Cohort Study, Longitudinal Study of Australian Children (LSAC); Australia</b></p> <p>Baseline N=4983, Analytic N (Wave 4)=4169 (Attrition: 16%); Power: NR</p> <p><b>Recruitment:</b> convenience sample</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49%</li> <li>Age: 4.8 (0.2) y</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMIZ 0.65 (1.00)</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In Australian children, there was a positive association between frequency of consumption of SSB and BMI z-scores, where each additional occurrence of SSB intake per day was associated with higher BMI z-scores.</p>	<p><b>Exposure of interest:</b> SSB intake (fruit juice, soft drink, or cordial; not including diet soft drinks or cordials)</p> <p><b>Comparators:</b> SSB intake (continuous; frequency of consumption per day)</p> <p>Other exposure measures: N/A</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Two survey questions (parent-report during face-to-face interview) on frequency of intake in previous 24hr</li> <li>At baseline (Wave 1, 2004), and every 2y (Waves 2-4: 2006, 2008, 2010)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSB intake at baseline: 1.7 (1.2) times consumed in previous 24hr</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (Wave 1, 2004), and every 2y (Waves 2-4: 2006, 2008, 2010)</li> <li>Height measured twice to nearest 0.1 cm using portable rigid stadiometer (average used in analysis)</li> <li>Weight measured to nearest 50g using glass bathroom scales</li> <li>Age- and sex-specific BMI z-scores (BMIZ) calculated using WHO Growth Standard for 6- to 60-month-old children and Growth Reference for 5- to 19-year-old children</li> </ul>	<p><b>BMIZ.</b> Multilevel growth model, <math>\beta</math> (95% CI)</p> <p><b>Change over 4 waves per each additional occurrence of SSB intake per day:</b></p> <p><b>0.015 (0.004, 0.025), <math>P&lt;0.01</math></b></p> <p><i>Using imputed maternal BMI data (20 imputations –21% missing before imputation)</i></p> <p><b>0.017 (0.007, 0.027), <math>P\leq 0.01</math></b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b></p> <p>Wave, mother's BMI, high-fat food intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure data collection tool not validated</li> <li>Exposure is frequency of SSB, not amount, and only represents 1, 24hr period, which may not represent usual intake</li> <li>Level of missing data is low but not specified whether it differed by exposure level</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>None reported</p>

**Mirmiran, 2015<sup>122</sup>**

**Prospective Cohort Study, Tehran Lipid and Glucose Study (TLGS), Iran**

Baseline N=621, Analytic N=327  
(Attrition: 47%); Power: NR

**Recruitment:** medical health centers in District No. 13 of Tehran

**Participant characteristics: children and adolescents**

- Total energy intake: ~2559 kcal/d
- Sex (female): 68%
- Age: 13.6 (3.7)y; Range: 6-18y
- Race/ethnicity: NR
- SES: NR
- Anthropometrics: BMI ~19.4 kg/m<sup>2</sup>
- Physical activity: NR
- Smoking: NR

**Summary of findings:**

In Iranian children and adolescents, when controlling for energy intake, higher SSB intake was significantly associated with increased abdominal obesity at 3.6y follow up. When looking at individual components of SSB intake, higher intake of sugar sweetened carbonated soft drinks was significantly associated with increased abdominal obesity at 3.6y follow up, but there was no significant association for fruit juice drinks.

**Exposure of interest:** SSB intake (sugar sweetened carbonated soft drinks (SSSDs), “did not differentiate between artificial non-caloric sweeteners and those containing caloric sugar e.g. fructose or sucrose”) and combined fruit juice drinks (both 100% fruit juice and sugar sweetened synthetic juice drinks that were not 100% juice)); 1 svg= 1 cup (250 mL)

**Comparators:** SSB intake (categorical; mL/d):

- Quartile 1 (Median 9.3)
- Quartile 2 (Median 32.0)
- Quartile 3 (Median 58.6)
- Quartile 4 (Median 142.2)

Other exposure measures: N/A

**Exposure assessment method and timing:**

- Validated semi-quantitative FFQ; represents usual dietary intake during the past year (parent-assisted if needed)
- At baseline

**Study beverage intake:** mL/d, Mean

- SSB intake: Boys, 98; Girls, 70
- Fruit juice drink and SSSD intake: NR

**Outcome assessment methods/timing:**

- At baseline, 3y follow-up (mean=3.6y)
- Weight measured to nearest 100 g using digital scale
- Height measured in standing position without shoes using stadiometer
- BMI calculated as kg/m<sup>2</sup>
- Waist circumference (WC) measured to nearest 0.5 cm at umbilicus using measuring tape
- Abdominal obesity: For children and adolescents, WC ≥90<sup>th</sup>% for age and sex according to national reference curves; for participants >18y, WC ≥91cm for women and ≥89cm for men

**Incident abdominal obesity,** Change per quartile increase, Logistic regression, OR (95% CI)

**SSB:**

Q1 (ref) vs  
Q2: 2.16 (0.82, 5.68)  
Q3: 1.86 (0.71, 4.84)  
Q4: 3.66 (1.40, 9.59)

**P for trend: 0.016**

**Fruit juice drink:**

Q1 (ref) vs  
Q2: 2.31 (0.95, 5.61)  
Q3: 0.88 (0.33, 2.35)  
Q4: 1.26 (0.48, 3.34)  
P for trend: 0.865

**SSSD:**

Q1 (ref) vs  
Q2: 1.57 (0.60, 4.06)  
Q3: 2.03 (0.78, 5.28)  
Q4: 3.78 (1.08, 13.27)

**P for trend: 0.043**

**TEI adjusted:** Yes

**Confounders accounted for:**

- Key confounders: sex, age, anthropometry at baseline, physical activity,
- Other factors considered: total energy intake, fiber

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity SES, smoking
- Other factors considered: timing, temporal use, sugar, protein, energy density, medications, supplements, alcohol

**Additional model adjustments:**

Family history of diabetes, tea and coffee, red and processed meat, fruits, vegetables

**Limitations:**

- Not all key confounders accounted for
- Exposure measured at baseline only
- Exposure not well defined
- No preregistered data analysis plan

**Funding sources:**

Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran



**Muckelbauer, 2016**<sup>123</sup>

**Secondary analysis of RCT**  
(Longitudinal analyses of intervention & control groups combined), Germany  
Analytic N=1987 (Overall trial attrition: ~8% ); Power: NR

**Recruitment:** elementary schools randomly select from deprived districts of two German cities (Dortmund and Essen)

**Participant characteristics: children participating in a 1yr, school-based intervention aimed at promoting water consumption to prevent overweight**

- Total energy intake: NR
- Sex (female): 53%
- Age: 8.3 (0.7) y
- Race/ethnicity: 44% Migrational background (child or parent born in foreign country)
- SES: NR
- Anthropometrics: BMI 17.2 (2.9) kg/m<sup>2</sup>; 76% Normal weight, 17% Overweight, 7% Obesity
- Physical activity: NR
- Smoking: NR
- Intervention group: 54%

#### Summary of findings:

Among children participating in a school-based intervention, higher increase in consumption of sugar-containing beverages was associated with greater increase in BMI and odds of obesity over a ~8mo school year. Soft drink intake was positively associated with increased BMI.

**Exposure of interest:** Sugar-containing beverage intake (SSBs combined intake of soft drinks, including lemonades and iced tea; and juices, including fruit drinks of any percentage fruit juice); 1 glass ~ 200 mL

**Comparator:** Sugar-containing beverage

- Continuous; glass/d
- Categorical (quintiles):
  - Q3 (ref): no or small change in beverage consumption
  - Q5: highest increase in beverage consumption

Other exposure measures: water

**Exposure assessment method and timing:**

- Semi-quantitative 24-hr recall questionnaire
- At baseline (start of school year), and end of same school year (mean follow up 8.2±0.2 mo)

**Study beverage intake:** glasses/d, Mean (SD)

- Sugar-containing beverages: 2.7 (2.4)
  - Soft drinks: 1.3 (1.7)
  - Juice: 1.4 (1.7)

**Outcome assessment methods/timing:**

- At baseline (start of school year), and end of same school year (mean follow up 8.2±0.2 mo)
- Height and weight measured in light clothes by trained study staff
- BMI calculated as kg/m<sup>2</sup>
- Weight categories (normal weight, overweight and obesity) defined according to recommendations of the International Obesity Task Force

**BMI**, kg/m<sup>2</sup>, Linear regression,  $\beta$  (95% CI)

**Mean change per glass/d increase:**

**SSBs: 0.02 (0.00, 0.03), P=0.011**

**Soft drinks: 0.02 (0.00, 0.04), P=0.019**

Juice: 0.01 (-0.01, 0.03), P=0.18

**BMI**, kg/m<sup>2</sup>, Linear regression,  $\beta$

**Mean change by quintile of bev intake:**

*Sugar-containing beverages*

Q3 (ref) vs:

Q4: 0.03

**Q5: 0.16 (0.06, 0.25)**

**P for trend: 0.014**

*Soft drinks:*

Q3 (ref) vs:

Q4: 0.06

Q5: 0.09

P for trend: 0.057

*Juice:*

Q3 (ref) vs:

Q4: 0.00

Q5: 0.05

P for trend: 0.82

**Overweight (including Obesity),**

Logistic regression, OR (95% CI)

SSBs: 0.99 (0.90, 1.09), P=0.83

Soft drinks: 0.99 (0.88, 1.12), P=0.89

Juice: 0.98 (0.86, 1.12), P=0.76

**Obesity**, Logistic regression, OR (95% CI)

**SSBs: 1.22 (1.04, 1.44), P=0.014**

Soft drinks: 1.17 (0.93, 1.48), P=0.19

**Juice: 1.29 (1.02, 1.61), P=0.030**

*When adjusting for baseline prevalence instead of BMI:*

SSBs: 1.13 (0.99, 1.30), P=0.064

Soft drinks: 1.16 (0.96, 1.39), P=0.13

**TEI adjusted:** No

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, anthropometry at baseline
- Other factors considered: N/A

**Confounders NOT accounted for:**

- Key confounders: SES, physical activity, smoking
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:**

Study arm, follow-up duration, water intake, baseline beverage intake, change in intake of other beverages

**Limitations:**

- Not all key confounders accounted for
- Exposure not well defined (multiple beverage types)
- Exposure data collection tool not validated and only represents previous day, not habitual intake
- No preregistered data analysis plan

**Funding sources:**

None received

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Olsen, 2012</b><sup>124</sup></p> <p><b>Prospective Cohort Study, Danish part of European Youth Heart Study (EYHS), Denmark</b></p> <p>Analytic N=359 (Attrition: NR ); Power: NR</p> <p><b>Recruitment:</b> proportionate two-stage cluster sample from schools in municipality of Odense, Denmark</p> <p><b>Participant characteristics: Danish 3<sup>rd</sup> grade children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~9.1 MJ/d</li> <li>• Sex (female): 56%</li> <li>• Age: ~9.6y (8-10y)</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI ~17.2 kg/m<sup>2</sup></li> <li>• Physical activity: Physical fitness ~3.0 W/kg</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In Danish children, liquid sucrose intake was not significantly associated with changes in waist circumference or BMI z-scores over 6 years, with or without adjusting for total energy intake.</p>	<p><b>Exposure of interest:</b> Liquid sucrose (carbonated, SSB with a sucrose content of 10% of volume and sugar-sweetened lemonade)</p> <p><b>Comparator:</b> Liquid sucrose intake (continuous; per 10g)</p> <p>Other exposure measures: N/A</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• 24hr dietary recall interview supplemented by a FFQ and a qualitative food record</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Liquid sucrose intake: ~21 g/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline (1997-1998), and ~6y follow-up (2003-2004)</li> <li>• Height measured to nearest 5 mm using a stadiometer</li> <li>• Weight measured to nearest 0.1 kg using a beam-scale type weight</li> <li>• Age- and gender-specific BMI z-scores (BMIZ) generated using LMS method</li> <li>• Waist circumference measured twice (mean was calculated) at the largest circumference of abdomen between ribs and trochanter major</li> </ul>	<p>Juice: 1.11 (0.93, 1.34), P=0.25</p> <p><b>WC, Change over 6 years</b>, cm, Linear regression, <math>\beta</math> (SE) TEI unadj: 0.140 (0.132), P=0.29 TEI adj: 0.151 (0.149), P=0.31</p> <p><b>BMIZ, Change over 6 years</b>, SD, Linear regression, <math>\beta</math> (SE) TEI unadj: 0.017 (0.016), P=0.30 TEI adj: 0.006 (0.018), P=0.74</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, SES, anthropometry at baseline, physical activity,</li> <li>• Other factors considered: total energy intake, sugar (solid sucrose)</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, race/ethnicity, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b></p> <p>Intake of complex carbohydrates, intake of fat, whether puberty started, school, fasting insulin level</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• 39% of original sample was excluded due to missing data—no information on how it may have varied across groups</li> <li>• Exposure measured only at baseline</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>Danish Heart Foundation; Danish Medical Research Council; Health Foundation; Danish Council for Sports Research; Foundation of 17–12–1981; Foundation in Memory of Asta Florida Bolding nee Andersen, Faculty of Health Sciences, University of Southern Denmark; Tryg Foundation</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Seo, 2015<sup>128</sup></b></p> <p><b>Prospective Cohort Study; Healthy, Energetic, Ready, Outstanding, Enthusiastic Schools (HEROES) Initiative (NRCT), United States</b> Baseline N=NR Analytic N=5309 (Attrition: NR%); Power: NR</p> <p><b>Recruitment:</b> 11 elementary or secondary schools in southern Indiana, northwestern Kentucky, and southeastern Illinois</p> <p><b>Participant characteristics: 4<sup>th</sup>-12<sup>th</sup> grade children participating in a school-based intervention</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 50%</li> <li>Age: 10.8 (3.2) y</li> <li>Race/ethnicity: White 81%, Nonwhite 19%</li> <li>SES: School lunch: 51% Eligible for free or reduced-price lunch</li> <li>Anthropometrics: BMI percentile, 68.4 (28.0)</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b> Among children participating in a school-based intervention, soda intake was significantly associated with higher odds of persistent overweight/obesity and deteriorated weight status compared to the persistent non-overweight status group.</p>	<p><b>Exposure of interest:</b> Soda intake</p> <p><b>Comparator:</b> Soda intake (continuous; times/d)</p> <p>Other exposure measures: N/A</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>"Yesterday, how many times did you drink a full serving of regular (not diet) soda?"</li> <li>At baseline, 6, 12, and 18mo follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Soda intake: NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 6, 12, and 18mo follow-up</li> <li>Height measured by two trained staff using a stadiometer</li> <li>Weight measured by two trained staff using a digital scale</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>Age- and sex-adjusted BMI percentiles and weight status categories based on 2009 CDC growth charts: Underweight (&lt;5<sup>th</sup>%), Normal (5<sup>th</sup>-84.9<sup>th</sup>%), Overweight (85<sup>th</sup>-94.9<sup>th</sup>%), Obesity (≥95<sup>th</sup>%)</li> <li>Weight status: Persistent non-overweight or non-obese (stayed normal or underweight during 18mo study period); Persistent overweight or obesity (stayed overweight or obese during 18mo study period); Deteriorated weight (moved from normal/underweight to ovwt/obesity then stayed in ovwt/obesity, or from overweight to obesity and then remained in obesity); Improved weight (those who lost weight and moved to and maintained normal/underweight status)</li> </ul>	<p><b>Weight Status, change during 18mo study period per continuous soda intake</b>, Logistic regression, OR (95% CI) <i>Persistent non-overweight</i> (n=2929, ref) vs.</p> <p><i>Persistent overweight/obesity</i> (n=1627): <b>1.07 (1.03, 1.11), P=0.0016</b></p> <p><i>Deteriorated weight (normal/underweight to ovwt/obesity, or overweight to obesity; n=364)</i> <b>1.08 (1.01, 1.15), P=0.0278</b></p> <p><i>Improved weight (ovrwt/obesity to normal, obesity to overweight; n=330)</i> 0.93 (0.85, 1.02), P=0.1356</p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: age, anthropometry at baseline</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, race/ethnicity, SES, physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> School (cluster)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No information on baseline N or attrition</li> <li>Exposure (soda intake) measured using single question representing previous day only and not well-defined</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b> Wellborn Baptist Foundation; National Research Foundation of Korea</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Shroff, 2014</b><sup>129</sup></p> <p><b>Prospective Cohort Study, Bogotá School Children Cohort, Colombia</b></p> <p>Baseline N=961, Analytic N=890 (Attrition: 7.4%); Power: NR</p> <p><b>Recruitment:</b> random selection from public primary schools in Bogotá, Colombia</p> <p><b>Participant characteristics: low- and middle-income school-aged children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: ~6440 kJ/d</li> <li>Sex (female): 51%</li> <li>Age: 8.6 (1.7) y</li> <li>Race/ethnicity: Born in Bogotá ~86%</li> <li>SES: Low ~43%; Mother's education ~8.6 yr</li> <li>Anthropometrics: BMIZ 0.12 (1.02); BMIZ&gt;1: 18%; BMIZ&gt;2: 4%</li> <li>Physical activity: Time playing outside ~17.3 hr/wk</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In low- and middle-income Colombian children, when controlling for energy intake, higher soda intake showed a significant linear trend with annual increases in BMI and waist circumference compared to children who never drank soda. There was no association between soda intake and skinfold thickness (subscapular:triceps ratio).</p>	<p><b>Exposure of interest:</b> Soda intake</p> <p><b>Comparators:</b> Soda intake (categorical):</p> <ul style="list-style-type: none"> <li>Never (ref)</li> <li>&lt;1/mo</li> <li>1/wk to 1/mo</li> <li>2-6/wk</li> <li>≥1/d</li> </ul> <p>Other exposure measures: N/A</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>FFQ (completed by mother) administered by trained dietitians 4-d dietary record completed by parents; represents usual dietary intake during the previous month</li> <li>At baseline (2006)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Soda intake at baseline: <ul style="list-style-type: none"> <li>Never to &lt;1/mo: 31%</li> <li>1/wk to 1/mo: 38%</li> <li>2-6/wk: 20%</li> <li>≥1/d: 10%</li> </ul> </li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (2006), 2007, and 2008</li> <li>Height measured by trained research staff using stadiometer</li> <li>Weight measured by trained research staff using a solar-powered electronic scale</li> <li>Triceps and subscapular skinfold thickness (SKF) was measured to nearest 0.5 mm with SlimGuide Skinfold Calipers</li> <li>Waist circumference measured to nearest 1 mm with non-extensible measuring tape at level of umbilicus according to standard protocol</li> </ul>	<p><b>BMI, annual change</b>, kg/m<sup>2</sup>, Linear regression, Mean (95% CI)</p> <p>Never (n=110, ref) vs</p> <p>&lt;1/mo (n=184): 0.06 (-0.06, 0.19)</p> <p>1/wk to 1/mo (n=356): 0.11 (0.00, 0.22)</p> <p>2-6/wk (n=187): 0.12 (-0.01, 0.25)</p> <p><b>≥1/d (n=98): 0.20 (0.04, 0.36)</b></p> <p><b>P trend: 0.01</b></p> <p><b>SKF, annual change</b>, Linear regression, Mean (95% CI)</p> <p>Never (n=110, ref) vs</p> <p>&lt;1/mo (n=184): 0.009 (-0.005, 0.023)</p> <p>1/wk to 1/mo (n=356): 0.001 (-0.011, 0.013)</p> <p>2-6/wk (n=187): 0.007 (-0.006, 0.020)</p> <p>≥1/d (n=98): 0.014 (-0.002, 0.030)</p> <p>P trend: 0.24</p> <p><b>WC, annual change</b>, cm, Linear regression, Mean (95% CI)</p> <p>Never (n=110, ref) vs</p> <p>&lt;1/mo (n=184): -0.1 (-0.8, 0.5)</p> <p>1/wk to 1/mo (n=356): 0.3 (-0.3, 0.9)</p> <p>2-6/wk (n=187): 0.3 (-0.4, 0.9)</p> <p>≥1/d (n=98): 0.6 (-0.1, 1.4)</p> <p><b>P trend: 0.04</b></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No information on how missing data were handled</li> <li>Exposure not well defined</li> <li>Exposure only measured at baseline</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>ASISA Research Fund at the University of Michigan</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Sichieri, 2013</b><sup>130</sup>  <b>Prospective Cohort Study (secondary analysis of RCT), Brazil</b>  Baseline N=NR, Analytic N=1134 (Attrition: NR%); Power: NR</p> <p><b>Recruitment:</b> 22 public schools in the metropolitan area of Rio de Janeiro, Brazil</p> <p><b>Participant characteristics: fourth graders participating in randomized trial</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): ~53%</li> <li>• Age: 10-11y</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI~18.2 kg/m<sup>2</sup></li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> <li>• Intervention group: NR</li> </ul> <p><b>Summary of findings:</b>  In Brazilian children, greater soda intake was significantly associated with increased BMI over 1 school year.</p>	<p><b>Exposure of interest:</b> Soda intake (colas and other sodas)</p> <p><b>Comparator:</b> Soda intake (continuous; glass/d)</p> <p>Other exposure measures: fruit juice (sweetened), water</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Single 24h recall, supplemented by a drinking frequency questionnaire representing usual intake</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Soda intake: ~0.6 glasses/d, ~250 ml/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline (beginning of school year) and end of same school year</li> <li>• Height measured without shoes to nearest cm using portable stadiometer</li> <li>• Weight measured to nearest 0.1 kg using portable scale</li> <li>• BMI calculated as kg/m<sup>2</sup></li> <li>• BMI z-score categories based on WHO</li> </ul>	<p><b>BMI</b>, kg/m<sup>2</sup>, Linear regression, <math>\beta</math> (95% CI)</p> <p><b>Change per glass/d increase:</b>  <b>0.11 (0.03, 0.25), P=0.002</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No information on baseline N or attrition</li> <li>• Exposure measured at baseline only</li> <li>• Exposure poorly defined</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Brazilian National Research Institute</p>

**Stoof, 2013<sup>132</sup>**

**Prospective Cohort Study,  
Amsterdam Growth and Health  
Longitudinal Study (AGAHLS), the  
Netherlands**

Baseline N=409, Analytic N=238  
(Attrition: 42%); Power: NR

**Recruitment:** secondary schools in  
Amsterdam and surrounding area

**Participant characteristics:  
adolescents**

- Total energy intake: ~10346 kJ/d
- Sex (female): 52%
- Age: 13 (0.6) y
- Race/ethnicity: NR
- SES: "all participants came from the same neighborhood and had a similar SES (moderate to high)"
- Anthropometrics: BMI~24.4 kg/m<sup>2</sup>
- Physical activity: ~625 MET x min/d
- Smoking: "few participants smoked"

**Summary of findings:**

In male adolescents, when controlling for energy intake, each additional serving of SSB intake at age 13y was significantly associated with higher %total fat and %trunk fat in adulthood ~24-30y later. There was no association between SSB intake and BMI. In female adolescents, there was no association between SSB intake and adult weight status.

**Exposure of interest:** sugar-containing beverages (SCB: carbonated and uncarbonated sugar-sweetened drinks such as soda, lemonade, iced tea, sports drinks and energy drinks, fruit drinks (diluted and sugar-sweetened fruit juices)). Did not include diet (low-energy) soft drinks, other non-caloric beverages, alcoholic beverages, milk and other liquid dairy products. (220 ml = 1 svg)

**Comparator:** SCB intake (continuous; svg/d)

Exposure assessment method and timing:

- Cross-check dietary history face-to-face interviews by a dietitian (parents also questioned on details of food items); represents usual intake during previous month
- At baseline (1976)

**Study beverage intake:**

- Sugar-containing beverages, ml/d, Mean (SD)
  - Female: 160 (137)
  - Male: 200 (191)

**Outcome assessment methods/timing:**

- At baseline, and 24 and/or 30y follow-up (2000 and/or 2006); if values were available for 2000 and 2006, the avg was used
- Weight and height measured by trained nurse according to standard procedures with participants wearing only underwear
- BMI calculated as kg/m<sup>2</sup>
- Total body fat mass, %total fat, and % trunk fat measured using DXA
- Overweight (BMI≥25 kg/m<sup>2</sup>) and obesity (BMI≥30 kg/m<sup>2</sup>) in adulthood defined according to WHO standards

**Associations between SSB intake  
(svg/d) at 13yo and body composition  
25-30y later;  $\beta$  (95% CI)**

**MALES (n=114)**

**% Total Fat:**

TEI unadj: 1.10 (-0.02, 2.21), P=0.05

**TEI adj: 1.14 (0.04, 2.23), P=0.04**

**% Trunk Fat:**

**TEI unadj: 1.57 (0.07, 3.08), P=0.04**

**TEI adj: 1.62 (0.14, 3.10), P=0.03**

**BMI:**

TEI unadj: 0.24 (-0.34, 0.81), P=0.42

TEI adj: 0.24 (-0.33, 0.82), P=0.41

**FEMALES (n=124)**

**% Total Fat:**

TEI unadj: -0.72 (-2.40, 0.97), P=0.40

TEI adj: -0.72 (-2.44, 1.01), P=0.41

**% Trunk Fat:**

TEI unadj: -0.77 (-2.88, 1.35), P=0.48

TEI adj: -0.85 (-3.02, 1.31), P=0.44

**BMI:**

TEI unadj: 0.44 (-0.37, 1.24), P=0.28

TEI adj: 0.43 (-0.39, 1.25), P=0.30

**TEI adjusted:** Yes and No

**Confounders accounted for:**

- Key confounders: sex, age, anthropometry at baseline, physical activity, smoking
- Other factors considered: total energy intake

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity, SES
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:** N/A

**Limitations:**

- Not all key confounders accounted for
- Attrition 42% without information on non-completers
- Exposure measured only at baseline
- Validation of exposure data collection tool not indicated
- No preregistered data analysis plan

**Funding sources:**

Dutch Heart Foundation; Dutch Prevention Fund; Dutch Ministry of Well Being and Public Health; Dairy Foundation on Nutrition and Health; Dairy Foundation on Nutrition and Health; Dutch Olympic Committee/Netherlands Sports Federation; Heineken Inc.

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Thurber, 2017<sup>134</sup></b></p> <p><b>Prospective Cohort Study, Longitudinal Study of Indigenous Children (LSIC), Australia</b></p> <p>Baseline N=1155, Analytic N=907 (Attrition: 21%); Power: NR</p> <p><b>Recruitment:</b> indigenous children from 11 diverse sites using purposive sampling</p> <p><b>Participant characteristics: Indigenous Australian children with normal BMI</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 50%</li> <li>Age: 62% ≤5y (3-6y); 34% &gt;5y (6-9y)</li> <li>Race/ethnicity: 88% Aboriginal</li> <li>SES, primary caregiver: 70% Not employed, 59% &lt; 12y education</li> <li>Anthropometrics: ~9% Overweight, 3% Obesity</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>Among Indigenous Australian children with normal baseline BMI, SSB intake was not significantly associated with changes in BMI 3 years later.</p>	<p><b>Exposure of interest:</b> SSB intake (soft drink, cordial, or sports drink – not diet)</p> <p><b>Comparators:</b> SSB intake (categorical):</p> <ul style="list-style-type: none"> <li>&lt;2 occasions on preceding day</li> <li>≥2 occasions on preceding day</li> </ul> <p>Other exposure measures: N/A</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Parent-report 24-hr recall; represents consumption from previous day</li> <li>At baseline (Wave 3), and annually for 3y (Waves 4-6)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSB intake: ≥2 occasions on preceding day, 31%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (Wave 3), and annually for 3y (Waves 4-6)</li> <li>Height measured without shoes using Soehnle Professional stadiometer</li> <li>Weight measured in light clothing using Homedics digital scale</li> <li>BMI calculated as kg/m<sup>2</sup></li> </ul>	<p><b>BMI, change over 3y</b>, per occasion of SSB intake on preceding day, Multilevel growth model, Mean (95% CI)</p> <p>≥2 (n=173): 1.2 (0.9, 1.5)</p> <p>&lt;2 (n=409): 0.9 (0.7, 1.1)</p> <p><b>BMI, change over 3y</b>, per occasion of SSB intake on preceding day, Multilevel growth model; %</p> <p><i>Decrease (mean annual BMIZ <math>\Delta</math> ≤0.3)</i></p> <p>≥2: 6.9%</p> <p>&lt;2: 13.7%</p> <p>P=NS (NR)</p> <p><i>No change (mean annual BMIZ <math>\Delta</math> -0.3-0.3)</i></p> <p>≥2: 60.7%</p> <p>&lt;2: 58.9%</p> <p>P=NS (NR)</p> <p><i>Increase (mean annual BMIZ <math>\Delta</math> ≥0.3)</i></p> <p>≥2: 32.4%</p> <p>&lt;2: 27.4%</p> <p>P=NS (NR)</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b></p> <p>Screen time, high-fat food consumption, screen time</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure data collection tool not validated</li> <li>Exposure assessment based on 1d, had no information on portion size</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>Australian National University; National Health and Medical Research Council of Australia</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Traub, 2018<sup>135</sup></b></p> <p><b>Secondary analysis of Baden-Württemberg Study (Cluster RCT—prospective analysis), Germany</b> Baseline N=NR, Analytic N=1733 (Attrition: NR%); Power: NR</p> <p><b>Recruitment:</b> primary schools in Baden-Württemberg, south-west Germany</p> <p><b>Participant characteristics: children participating in school intervention</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 49%</li> <li>• Age: 7.08 (0.63) y</li> <li>• Race/ethnicity: 31% history of migration</li> <li>• SES: 10% single parent, 32.4% tertiary family education level, 12.6% household income ≤ 1750 €</li> <li>• Anthropometrics: 10% Overweight, 4% Obesity, 8% Abdominal Obesity</li> <li>• Physical activity: 27% Physically active ≥4 d/wk ≥60 min/d; 69% Play outside &gt; 60 min/d</li> <li>• Smoking: 10% Maternal during pregnancy</li> <li>• Intervention group: 55%</li> </ul> <p><b>Summary of findings:</b> In children participating in a school-based intervention, soft drink intake was not associated with abdominal obesity, overweight, or obesity at 1y follow up, nor was it related to changes in waist-to-height ratio, weight, or BMI percentile during that year.</p>	<p><b>Exposure of interest:</b> Soft drink intake</p> <p><b>Comparator:</b></p> <ul style="list-style-type: none"> <li>• Soft drink intake ≤1/week (Ref)</li> <li>• Soft drink intake &gt;1/week</li> </ul> <p>Other exposure measures: N/A</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Questions on soft drinks at school and outside school assess on a 6-point Likert scale; represents frequency of intake during the week</li> <li>• At baseline, 1y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Soft drink intake: 25% &gt;1 time/wk <ul style="list-style-type: none"> <li>◦ At school: 7%</li> <li>◦ Outside school: 24%</li> </ul> </li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 1y follow-up</li> <li>• Height measured by trained staff to the nearest 0.1 cm using stadiometer</li> <li>• Weight measured by trained staff to the nearest 0.1 kg using electric calibrated and balanced scale</li> <li>• Waist circumference measured by trained staff to the nearest 0.1 cm using a flexible metal tape</li> <li>• Age- and gender specific BMI percentile cut-offs based on German reference data: Overweight (&gt;90<sup>th</sup>%) and Obese (&gt;97<sup>th</sup>%)</li> <li>• Waist-to-height ratio calculated</li> <li>• Abdominal obesity: defined as waist-to-height ratio ≥0.5</li> </ul>	<p><b>Abdominal Obesity at 1y follow up,</b> Generalized linear mixed effects regression, OR (95% CI) Soft drink &gt;1/wk: 1.46 (0.92, 2.32), P=0.108</p> <p><b>Overweight at 1y follow up,</b> Generalized linear mixed effects regression, OR (95% CI) Soft drink &gt;1/wk: 1.29 (0.84, 1.96), P=0.246</p> <p><b>Obesity at 1y follow up,</b> Generalized linear mixed effects regression, OR (95% CI) Soft drink &gt;1/wk: 1.57 (0.82, 3.03), P=0.177</p> <p><b>Changes in Waist-to-Height Ratio,</b> Linear mixed effects regression, β (SE) Soft drink &gt;1/wk: -0.01 (0.15), P=0.966</p> <p><b>Changes in Weight,</b> Linear mixed effects regression, β (SE) Soft drink &gt;1/wk: -0.08 (0.09), P=0.385</p> <p><b>Changes in BMI%,</b> Linear mixed effects regression, β (SE) Soft drink &gt;1/wk: -0.75 (0.70), P=0.282</p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, SES, anthropometry at baseline</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> School, migration status, assignment to intervention or control group</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No information on baseline N or attrition</li> <li>• Exposure not well defined</li> <li>• Exposure data collection tool not validated</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b> Baden-Württemberg Stiftung</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Wheaton, 2015</b><sup>138</sup>  <b>Prospective Cohort Study, Longitudinal Study of Australian Children (LSAC), Australia</b>  Baseline N=4983, Analytic N=4169 (Attrition: 16%); Power: NR</p> <p><b>Recruitment:</b> sampling frame drawn from Medicare Australia enrollment database</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49%</li> <li>Age: 4.8 (0.2) y</li> <li>Race/ethnicity: 96% born in Australia</li> <li>SES: disadvantaged areas "underrepresented"</li> <li>Anthropometrics: BMIZ: 0.66 (0.99); Weight status: Thinness/normal 68%, Overweight 23%, Obese 9%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, SSB intake was not significantly associated with changes in weight status at 2, 4, or 6y follow-up. Children who were overweight or had obesity at both baseline and 6y follow up were more likely to consume SSBs than children who were normal weight at both baseline and 6y follow up.</p>	<p><b>Exposure of interest:</b> SSB intake (fruit juice; non-diet soft drink or cordial)</p> <p><b>Comparators:</b> SSB intake (categorical):</p> <ul style="list-style-type: none"> <li>0=Normal to normal (ref)</li> <li>1=Normal to ovrwt/obese</li> <li>2=Ovrwt/obese to ovrwt/obese</li> <li>3= Ovrwt/obese to normal</li> </ul> <p>Other exposure measures: N/A</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Parent-report survey questions; represents intake during previous 24hr</li> <li>At wave 1 (age 4-5y), and biennial waves 2 and 3 (age 6-8y, 8-9y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSB intake: NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At wave 1 (age 4-5y), and biennial waves 2-4 (age 6-8y, 8-9y, 10-11y)</li> <li>Weight measured to nearest 50 g using Salter Australia bathroom scales</li> <li>Height measured twice to nearest 0.1 cm using portable rigid stadiometer</li> <li>Age- and sex-specific BMI z-score calculated according to WHO Growth Standard for children from birth-60mo</li> <li>Weight status categories based on WHO cut-off points: overweight (BMI &gt;25 kg/m<sup>2</sup>), obese (BMI&gt;30 kg/m<sup>2</sup>).</li> </ul>	<p><b>Change in Weight Status</b>, Logistic regression, RRR (SE)  <b>Wave 1 (age 4-5y) to Wave 2 (age 6-7y)</b>  0 (normal to normal; ref) vs  1 (normal to ovrwt/ob): 0.95 (0.07), P=0.52  2 (ovrwt/ob to ovrwt/ob): 1.05 (0.05), P=0.28  3 (ovrwt/ob to normal): 1.04 (0.06), P=0.51</p> <p><b>Wave 1 (age 4-5y) to Wave 3 (age 8-9y)</b>  0 (normal to normal; ref) vs  1 (normal to ovrwt/ob): 0.97 (0.06), P=0.58  2 (ovrwt/ob to ovrwt/ob): 1.09 (0.05), P=0.07  3 (ovrwt/ob to normal): 0.95 (0.06), P=0.40</p> <p><b>Wave 1 (age 4-5y) to Wave 4 (10-11y)</b>  0 (normal to normal; ref) vs  1 (normal to ovrwt/ob): 0.97 (0.05), P=0.57  <b>2 (ovrwt/ob to ovrwt/ob): 1.13 (0.06), P=0.01</b>  3 (ovrwt/ob to normal): 0.93 (0.06), P=0.21</p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Mother's and father's BMI</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure data collection tool not validated</li> <li>Unclear if % missing data was equal across exposure groups</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  Australian National Health and Medical Research Council; Australian National Heart Foundation; NIH; NHMRC Centre for Research Excellence in Obesity Policy and Food Systems; Deakin University</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Whetstone, 2012<sup>59</sup></b>  <b>Prospective Cohort Study, North Carolina Health and Wellness Trust Fund programs (NRCT), United States</b>  Baseline N=2487, Analytic N=1144 (Attrition: 54%); Power: NR</p> <p><b>Recruitment:</b> community-originated local program</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 51.7%</li> <li>• Age, mean (SD): 9.5 (4.1) y, Range: 4.1-18.6</li> <li>• Race/ethnicity: Caucasian 64.7%, African-American 35.3%, Hispanic/Latino origin 2.6%</li> <li>• SES: NR</li> <li>• Anthropometrics, mean (SD): BMI z-score: 0.82 (1.13); Weight status: underweight=1.6%, healthy weight=55.0%, overweight=16.9%, obese=26.6%</li> <li>• Physical activity: mean number of days of exercise or physical activity per week: 4.49</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Among children with overweight/obesity, those who decreased their soda intake were more likely to reduce their BMIZ compared to those who did not change their soda intake. Soda intake was not significantly associated with changes in weight status.</p>	<p><b>Exposure of interest:</b> Change in soda intake (decreased intake of non-diet sodas and sweetened beverages)</p> <p><b>Comparator:</b> No change in soda intake</p> <p>Other exposure measures: milk</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Unvalidated health survey completed by parents (if child was grade K-5) or self (if child was grade 6-12); represents typical daily consumption</li> <li>• At baseline and every 6 months during follow-up period; average follow-up 20.5y (range: 8-29mo)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Frequency of soda intake: did not drink, 39.6%</li> <li>• Frequency of sweetened beverage intake: did not drink: 14.9%, ≥3 drinks/d: 31.1%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline and every 6 months during follow-up period; average follow-up 20.5y (range: 8-29mo)</li> <li>• Height measured by trained staff, stadiometers recommended but alternative instructions for triangular ruler and metal tape measure provided</li> <li>• Weight measured by trained staff using balance beam or digital scale</li> <li>• BMI z-score (BMIZ) calculated using approach on CDC website</li> <li>• Weight status were age- and gender-specific CDC designations: underweight (BMI&lt;5%), healthy weight (5%≤BMI&lt;85%), overweight (85%≤BMI&lt;95%), obese (BMI≥95%)</li> </ul>	<p><b>Weight Status</b>, Percentage of <i>overweight/obese children</i> who lowered their weight status category (subgroup n NR), Chi-square difference  Did not decrease soda vs Decreased soda: : 22.2% vs 30.6%, P&gt;0.05</p> <p><b>BMIZ</b>, Change in BMIZ among <i>overweight/obese children</i> (subgroup n NR), ANOVA  <b>Did not decrease soda vs Decreased soda: -0.09 vs -0.20, P=0.038</b></p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, anthropometry at baseline</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Grantee</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Participants hand-selected by grantee to be “representative”</li> <li>• Exposure not clearly defined; tool not validated</li> <li>• Subgroup analyses reported; Results from full sample NR; no preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  North Carolina Health and Wellness Trust Fund Commission</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b><u>Yiotaldiotariotam, 2013</u></b><sup>139</sup></p> <p><b>Secondary analysis of Dutch Obesity Intervention in Teenagers (DOiT), the Netherlands</b></p> <p>Baseline N=NR, Analytic N=1108 (Attrition: NR); (Attrition for original trial ~18%) Power: NR</p> <p><b>Recruitment:</b> 18 prevocational secondary schools in the Netherlands</p> <p><b>Participant characteristics: adolescents participating in an 8mo school-based behavioral intervention</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 50%</li> <li>• Age: ~12.7y (Range 12-13y)</li> <li>• Race/ethnicity: 12% Non-Western immigrants</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI ~18.3 kg/m<sup>2</sup>; 14% Overweight/Obese</li> <li>• Physical activity: Active transport to/from school ~30 min/d</li> <li>• Smoking: NR</li> <li>• Intervention group: 57%</li> </ul> <p><b>Summary of findings:</b></p> <p>Among adolescents participating in a school-based behavioral intervention program, sugar-containing beverage consumption mediated the effect of intervention on weight loss, such that a decrease in SSB consumption led to decreased BMI. SSB intake was not significantly associated with changes in waist circumference or skinfold thickness. There was no significant association between soft drink intake and BMI, waist circumference, or skinfold thickness.</p>	<p><b>Exposure of interest 1:</b> Sugar-containing beverages (SSB)</p> <p><b>Exposure of interest 2:</b> Soft drinks (fizzy drinks, lemonade, ice tea, energy drinks; not including diet drinks)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>• SSB intake (continuous; L/d)</li> <li>• Soda intake (continuous; L/d)</li> </ul> <p>Other exposure measures: fruit juice</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Validated questionnaire (self-report)</li> <li>• At baseline, 8, 12, and 20mo</li> </ul> <p><b>Study beverage intake:</b> L/d, Median</p> <ul style="list-style-type: none"> <li>• SSB: ~0.94</li> <li>• Soft drinks: ~0.68</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 8, 12, and 20mo</li> <li>• Weight and height measured by trained research assistants with a calibrated electronic flat scale and a portable stadiometer</li> <li>• BMI calculated as kg/m<sup>2</sup></li> <li>• Weight status categories based on International Obesity Task Force cut-off values</li> <li>• Waist circumference (WC) in cm measured by a flexible band</li> <li>• Skinfold thickness (triceps, biceps, subscapular, suprailiac) measured using Harpender skin fold caliper and summed</li> </ul>	<p><b>BMI</b>, kg/m<sup>2</sup>, Latent growth model, <math>\beta</math> (95% CI)</p> <p><b>SSB: 0.10 (0.01, 0.13)</b></p> <p>Soft drinks: 0.15 (-0.25, 0.32)</p> <p><b>WC</b>, cm, Latent growth model, <math>\beta</math> (95% CI)</p> <p>SSB: 0.06 (-0.07, 0.19)</p> <p>Soft drinks: 0.07 (-0.11, 0.24)</p> <p><b>Sum of skinfolds</b>, mm, Latent growth model, <math>\beta</math> (95% CI)</p> <p>SSB: 0.002 (-0.56, 0.61)</p> <p>Soft drinks: 0.02 (-0.62, 0.77)</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Unclear if post-exposure variables impacted selection into study</li> <li>• No information on baseline N or attrition</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b></p> <p>World Cancer Research Fund; Netherlands Heart Foundation; Netherlands Organization for Health Research and Development; EMGO Institute</p>

## **Zheng, 2014<sup>140</sup>**

**Prospective Cohort Study, European Youth Heart Study (EYHS), Denmark**  
Baseline N=590, Analytic N=187 and 283 (Attrition: 52-68%); Power: NR

**Recruitment:** schools in Odense, Denmark

### **Participant characteristics: children**

- Total energy intake: ~9.3 MJ/d
- Sex (female): 56%
- Age: ~9.6y
- Race/ethnicity: NR
- SES: 57% Low (elementary, high school, or vocational education)
- Anthropometrics: BMI ~17.3 kg/m<sup>2</sup>
- Physical activity: 55% Active (regular exercise)
- Smoking: NR

### **Summary of findings:**

In 9 year-old Danish children, when controlling for energy intake, SSB intake at 9y and 15y was not significantly associated with changes in BMI, waist circumference, or skinfold measurements from 9-15y or 15-21y. When TEI was not adjusted, SSB intake at 15y was significantly associated with greater BMI increase and greater WC increase from 15-21y of age, and an increase in SSB intake from 9-15y was significantly associated with an increase in WC from 15-21y.

**Exposure of interest:** SSB intake (regular soft drinks, fruit drinks, and cordials sweetened with caloric sweeteners); 1 svg=12oz

**Comparators:** SSB intake (categorical):

- Non-consumer, ≤1, >1 svg/d
- No change, decrease, increase

Other exposure measures: N/A

### Exposure assessment method and timing:

- 24h recall face-to-face interview supplemented with a qualitative food record of same day completed by children with parental assistance
- At baseline (age 9), and 6y follow-up (age 15)

### **Study beverage intake:**

- SSB intake at 9y: 47% Non-consumer, 40% ≤1 svg/d, 13% >1 svg/d
- SSB intake at 15y: 50% Non-consumer, 24% ≤1 svg/d, 26% >1 serv/d
- A higher proportion of boys than girls consumed SSB at 1<sup>st</sup> follow up (age 15y, P=0.003)

### **Outcome assessment methods/timing:**

- At baseline (age 9), with 6y (age 15) and 12y (age 21) follow-up
- Height measured bare feet to nearest 5mm using stadiometer
- Weight measured to nearest 0.1 kg using beam balance scale
- BMI calculated as kg/m<sup>2</sup>
- Waist circumference (WC) measured twice with metal anthropometric tape (mean was used)

Sum of 4 skinfolds (Σ4SF) obtained by adding average skinfolds of 4 sites (biceps, triceps, subscapular, and suprailiac) that were measured in duplicate with Harpenden fat calipers

**BMI**, kg/m<sup>2</sup>, Linear regression, β (SE)

### **Change from 9–21y with SSB intake at 9y**

None (n=134, ref) vs  
≤1 svg/d (n=112): 0.53 (0.55), P=0.34  
>1 svg/d (n=37): 1.42 (0.68), P=0.29

### **Change from 15–21y with SSB intake at 15y**

None (n=94, ref) vs  
≤1 svg/d (n=43): 0.69 (0.57), P=0.23  
>1 svg/d (n=50): 0.97 (0.56), P=0.09

### **Change from 15–21y with SSB intake at 15y (NOT adjusted for TEI)**

None (n=94, ref) vs  
≤1 svg/d (n=43): 0.66 (0.56), P=0.24  
**>1 svg/d (n=50): 0.92 (0.54), P=0.046**

### **Change from 15–21y with change in SSB intake from 9-15y**

No change (n=45, ref) vs  
Decrease (n=64): 0.38 (0.61), P=0.53  
Increase (n=78): 1.00 (0.59), P=0.11

### **Change from 15–21y with change in SSB intake from 9-15y (NOT adjusted for TEI)**

No change (n=45, ref) vs  
Decrease (n=64): 0.38 (0.59), P=0.51  
Increase (n=78): 0.91 (0.57), P=0.09

**WC**, cm, Linear regression, β (SE)

### **Change from 9–21y with SSB intake at 9y**

None (n=134, ref) vs  
≤1 svg/d (n=112): 0.98 (1.3), P=0.46  
>1 svg/d (n=37): 0.80 (2.02), P=0.69

### **Change from 15–21y with SSB intake at 15y**

None (n=94, ref) vs  
≤1 svg/d (n=43): 2.58 (1.50), P=0.09  
>1 svg/d (n=50): 2.72 (1.51), P=0.07

### **Change from 15–21y with SSB intake at 15y (NOT adjusted for TEI)**

None (n=94, ref) vs  
≤1 svg/d (n=43): 2.57 (1.49), P=0.09  
**>1 svg/d (n=50): 2.69 (1.45), P=0.04**

**TEI adjusted:** Yes and No

The data on “Change from 9-21y with SSB intake at 9y” (for BMI, WC, and SF) did not adjust for TEI.

All other analyses provide both TEI-adjusted and non-adjusted data.

### **Confounders accounted for:**

- Key confounders: sex, age, SES, anthropometry at baseline, physical activity
- Other factors considered: total energy intake

### **Confounders NOT accounted for:**

- Key confounders: race/ethnicity, smoking
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

### **Additional model adjustments:**

Pubertal status, baseline SSB intake (model examining change in SSB intake 9-15y ONLY)

### **Limitations:**

- Not all key confounders accounted for
- No preregistered data analysis plan

### **Funding source:**

NR

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
		<p><b>Change from 15–21y with change in SSB intake from 9–15y</b>            No change (n=45, ref) vs            Decrease (n=64): 0.83 (1.61), P=0.75            Increase (n=78): 3.25 (1.53), P=0.07  <b>Change from 15–21y with change in SSB intake from 9–15y (NOT adjusted for TEI)</b>            No change (n=45, ref) vs            Decrease (n=64): 0.87 (1.55), P=0.57  <b>Increase (n=78): 2.72 (1.53), P=0.04</b></p> <p><b><math>\Sigma 4SE</math></b>, mm, Linear regression, <math>\beta</math> (SE)  <b>Change from 9–21y with SSB intake at 9y</b>            None (n=134, ref) vs  <math>\leq 1</math> svg/d (n=112): 0.76 (5.68), P=0.79  <math>&gt; 1</math> svg/d (n=37): 0.98 (3.63), P=0.79  <b>Change from 15–21y with SSB intake at 15y</b>            None (n=94, ref) vs  <math>\leq 1</math> svg/d (n=43): 1.37 (3.94), P=0.73  <math>&gt; 1</math> svg/d (n=50): 2.95 (3.92), P=0.45  <b>Change from 15–21y with change in SSB intake from 9–15y</b>            No change (n=45, ref) vs            Decrease (n=64): 4.03 (4.09), P=0.33            Increase (n=78): 4.60 (4.09), P=0.26  <i>Sum of skinfold data were also NS when TEI was not adjusted for</i></p>	

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Zheng, 2015<sup>1</sup></b>  <b>Prospective Cohort Study, Childhood Asthma Prevention Study, Australia</b>  Baseline N=237 Analytic N=158 (Attrition: 33.3%); Power: NR</p> <p><b>Recruitment:</b> pregnant women from antenatal clinics</p> <p><b>Participant characteristics: 8yo children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean ~8.0 MJ/d</li> <li>Sex (female): 48%</li> <li>Age: Mean ~8.0y</li> <li>Race/ethnicity: Mother born in Australia/New Zealand ~78%; Father born in Australia/New Zealand ~73%</li> <li>SES: Maternal education level &gt;12y ~55%; Paternal education level &gt;12y ~58%; Living in disadvantaged area ~20%</li> <li>Anthropometrics: BMI z-score, Mean (SD): 0.4(1.0); Overweight/obese 27.2%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> <li>Intervention group: 54.9%</li> </ul> <p><b>Summary of findings:</b>  In children, SSB consumption was significantly associated with increases in BMIZ and %BF.</p>	<p><b>Exposure of interest:</b> SSB intake (regular soft drinks, fruit drinks, cordials, and sugar-sweetened sport drinks)</p> <p><b>Comparator:</b> SSB intake (100 g/d) modeled continuously</p> <p>Other exposure measures: milk, water, 100% fruit juice, diet drinks, and liquid energy (energy from all beverages)</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Three 24-hr dietary recalls via phone using multiple pass approach completed by children with parental assistance; Represents usual dietary intake on nonconsecutive weekdays and weekends</li> <li>At 1y follow-up (age 9y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSB intake at baseline (g/d), Median: ~210</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>Baseline (age 8y), and 3.5y follow-up (age 11.5y)</li> <li>Weight measured to nearest 0.1kg</li> <li>Height measured using stadiometer</li> <li>Age- and sex-specific BMI z-scores (BMIZ) calculated using 2000 CDC growth charts</li> <li>Percentage body fat (%BF) measured by bioimpedance analysis</li> </ul>	<p><b>BMIZ</b>, Linear regression  <b>Change per 100 g/d increase, <math>\beta</math> (SE):</b>  <b>TEI unadj: 0.08 (0.03), P=0.02</b>  <b>TEI adj: 0.10 (0.03), P=0.003</b>  <b>Change per quartile (dose response):</b>  <b>P for trend=0.01</b></p> <p><b>%BF</b>, Linear regression  <b>Change per 100 g/d increase, <math>\beta</math> (SE):</b>  <b>Bev EI unadj: 0.92 (0.31), P=0.004</b>  <b>Bev EI adj: 1.04 (0.32), P=0.001</b>  <b>Change per quartile (dose response):</b>  <b>P for trend=0.005</b></p>	<p><b>TEI adjusted:</b> Yes and no</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Maternal age at birth, presence of gestational diabetes, exclusive breastfeeding at 3mo, pubertal status, randomization group (omega-3 fatty acid dietary supplementation and house dust mite reduction)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Anthropometric measures not taken at same time as dietary data</li> <li>Exposure data collected at 1 time to represent 3.5y period</li> </ul> <p><b>Funding sources:</b>  National Health and Medical Research Council of Australia; Cooperative Research Centre for Asthma; New South Wales Department of Health; Children's Hospital Westmead</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Zheng, 2015<sup>62</sup></b>  <b>Prospective Cohort Study, Healthy Start Study (RCT), Denmark</b>  Baseline N=552 Analytic N=352 (Attrition: 36.2%); Power: NR</p> <p><b>Recruitment:</b> Danish National Birth Register</p> <p><b>Participant characteristics: normal weight children at high-risk of overweight</b></p> <ul style="list-style-type: none"> <li>Total energy intake, MJ/d, Mean (SD): 4.97 (0.95)</li> <li>Sex (female): 45.2%</li> <li>Age: 4.1 (1.1) y</li> <li>Race/ethnicity: NR</li> <li>SES: Maternal education level, Tertiary or above: 78.0%; Paternal education level, Tertiary or above: 61.0%; Parents divorced 5.6%</li> <li>Anthropometrics: Mean (SD), Body weight (kg): 18.0 (3.3); BMI z-score: 0.3 (0.9)</li> <li>Physical activity: High 59.2%</li> <li>Smoking: NR</li> <li>Intervention group: 46.0%</li> </ul> <p><b>Summary of findings:</b>  In children, when controlling for energy intake, increasing sugary drink intake was associated with increased BMIZ, but was not significantly associated with changes in body weight.</p>	<p><b>Exposure of interest:</b> Sugary drink intake (sugar-sweetened carbonated drinks, fruit-flavored drinks, fruit juices)</p> <p><b>Comparator:</b> Sugary drink intake (100 g/d) modeled continuously</p> <p>Other exposure measures: milk, water, diet drinks</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>4-d dietary record completed by parents; represents dietary intake on both weekdays and weekends</li> <li>At baseline, 1.5y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Sugary drink intake at baseline (g/d), Mean (SD): 92.0 (107.0)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 1.5y follow-up</li> <li>Height measured using stature meter</li> <li>Weight measured using mechanical weight or beam-scale</li> <li>Age- and sex-specific BMI z-scores (BMIZ) calculated using Lambda-Mu-Sigma method</li> </ul>	<p><i>Nutrient Residual Model</i> (includes beverage intake residuals and total energy intake)  <b>BMIZ</b>, Linear regression  <b>Change per 100 g/d increase:</b>  B: 0.05, SE: 0.03, P=0.10</p> <p><b>Body weight</b>, Linear regression  <b>Change per 100 g/d increase:</b>  B: 0.10, SE: 0.07, P=0.08</p> <p><i>Energy Partition Model</i> (includes absolute amount of individual beverage intake and energy from non-beverage sources)  <b>BMIZ</b>, Linear regression  <b>Change per 100 g/d increase:</b>  <b>B: 0.06, SE: 0.03, P=0.04</b></p> <p><b>Body weight</b>, Linear regression  <b>Change per 100 g/d increase:</b>  B: 0.10, SE: 0.07, P=0.05</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Intervention allocation, parents divorced, number of siblings living with the child, maternal pre-pregnancy overweight</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 36% without information on non-completers</li> <li>No preregister analysis plan</li> </ul> <p><b>Funding sources:</b>  None</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Zheng, 2015<sup>61</sup></b>  <b>Prospective Cohort Study, European Youth Heart Study (EYHS), Denmark</b>  Baseline N=590, Analytic N=358 (Attrition: 39%); Power: NR</p> <p><b>Recruitment:</b> schools in Odense, Denmark</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: 9.1 (2.3) MJ/d</li> <li>Sex (female): 56%</li> <li>Age: 9.6 (0.4) y</li> <li>Race/ethnicity: NR</li> <li>SES: 47% Low (elementary, high school, or vocational education)</li> <li>Anthropometrics: BMI 17.2 (2.3) kg/m<sup>2</sup>; BMIZ 0.4 (1.1)</li> <li>Physical activity: 55% Active (regular exercise)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In Danish children, SSB intake at 9y was significantly associated with greater increase in both BMI and sum of skinfold thicknesses from age 9-15y when TEI was not adjusted for and also when only energy from non-beverage sources was adjusted for. The relationship was no longer significant when TEI was adjusted for.  SSB intake at 9y was not associated with change in WC from age 9-15y.</p>	<p><b>Exposure of interest:</b> SSB intake (regular soft drinks, lemonade, or fruit-flavored drinks)</p> <p><b>Comparator:</b> SSB intake (100g/d) modeled continuously</p> <p>Other exposure measures: water, milk, fruit juice, coffee/tea</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>One 24h recall face-to-face interview supplemented with parent-assisted food record; represents food intake</li> <li>At baseline (age 9)</li> </ul> <p><b>Study beverage intake:</b> g/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>SSB intake: 154.0 (204.9)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (age 9), and 6y follow-up (age 15)</li> <li>Height measured bare feet to nearest 5mm using stadiometer</li> <li>Weight measured to nearest 0.1 kg using beam balance scale</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>Age- and sex-specific BMI z-score (BMIZ) generated using the least mean squares method</li> <li>Waist circumference (WC) measured twice with metal anthropometric tape (mean was used)</li> <li>Sum of 4 skinfolds (<math>\Sigma</math>4SF) obtained by adding average skinfolds of 4 sites (biceps, triceps, subscapular, and suprailiac) that were measured in duplicate with Harpenden fat calipers</li> </ul>	<p><i>Base Model</i> (Model 1 in paper) adjusted for confounders listed to the right, but did not adjust for TEI</p> <p><i>Standard Multivariate Model</i> (Model 2 in paper) adjusted for TEI</p> <p><i>Energy Partition Model</i> (Model 3 in paper) included energy-containing beverages only (ie, excluded water) and adjusted for energy from non-beverage sources.</p> <p><b>Change in BMI age 9-15y:</b> kg/m<sup>2</sup>, Per 100 g/d increase, Linear regression, <math>\beta</math> (SE) (n=314)  Base Model: <b>0.05 (0.02), P=0.02</b>  TEI adjusted: 0.05 (0.02), P=0.06  Energy Partition: <b>0.05 (0.02), P=0.01</b></p> <p><b>Change in WC age 9-15y:</b> Per 100 g/d increase, Linear regression, <math>\beta</math> (SE) (n=314)  Base Model: 0.22 (0.15), P=0.14  TEI adjusted: 0.30 (0.15), P=0.18  Energy Partition: 0.25 (0.15), P=0.09</p> <p><b>Change in <math>\Sigma</math>4SF age 9-15y:</b> mm, Per 100 g/d increase, Linear regression, <math>\beta</math> (SE) (n=308)  Base Model: <b>0.86 (0.37), P=0.02</b>  Standard Model: 0.94 (0.39), P=0.06  Energy Partition: <b>0.88 (0.37), P=0.02</b></p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Pubertal status, Sex x SES, individual beverage intakes, energy from non-beverage sources</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure only measured once (at baseline)</li> <li>Exposure measured with single 24h dietary recall—may not reflect habitual intake</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NR</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Zulfigar, 2019</b><sup>141</sup></p> <p><b>Prospective Cohort Study, Longitudinal Study of Australian Children (LSAC), Australia</b></p> <p>Baseline N=4386, Analytic N=2389 (Attrition: 46% for these analyses; true LSAC birth cohort attrition ~26%); Power: NR</p> <p><b>Recruitment:</b> sampling frame drawn from Medicare Australia enrollment database</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49%</li> <li>Age: ~4.2y</li> <li>Race/ethnicity: 58% Australian, 30% Immigrants from high-income countries, 12% Immigrants from low/middle-income countries</li> <li>SES: Socioeconomic position: 24% High, 51% Middle, 24% Low</li> <li>Anthropometrics: ~22% Overweight/Obese</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In children, SSB intake was not associated with odds of overweight/obesity in boys or girls.</p>	<p><b>Exposure of interest:</b> SSB intake (no definition given, but could use definition in Wheaton, 2015 'SSBs: fruit juice; non-diet soft drink or cordial')</p> <p><b>Comparator:</b> SSB intake (categorical):</p> <ul style="list-style-type: none"> <li>None (ref)</li> <li>≥ 1/d</li> </ul> <p>Other exposure measures: N/A</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Parent report during waves 1-3, child report on computer-based study instrument at wave 4; represents intake during previous 24hr</li> <li>At wave 1 (age 4-5y), and biennial waves 2-4 (age 6-8y, 8-9y, 10-11y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSB intake: Highest intake shown in girls from low/middle-income countries from 4-9y of age</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At wave 1 (age 4-5y), and biennial waves 2-4 (age 6-8y, 8-9y, 10-11y)</li> <li>Weight measured to nearest 50 g using Salter Australia bathroom scales</li> <li>Height measured to nearest 0.1 cm using portable rigid stadiometer</li> <li>Age- and sex-specific BMI calculated</li> <li>Child overweight/obese defined according to International Obesity Task Force age-and-sex-specific criteria (cut off points of 25 and 30 kg/m<sup>2</sup> for overweight and obesity, respectively – extrapolated to children)</li> </ul>	<p><b>Overweight/Obesity at age 10-11y</b>, per daily SSB intake, Logistic regression, OR (95% CI)</p> <p><b>Boys (n=2115)</b></p> <p>None (ref) vs v≥ 1/d: 1.01 (0.80, 1.29)</p> <p><b>Immigrant Boys (n=883)</b></p> <p>None (ref) vs ≥ 1/d: 1.01 (0.80, 1.28)</p> <p><b>Girls (n=2000)</b></p> <p>None (ref) vs ≥ 1/d: 1.08 (0.87, 1.35)</p> <p><b>Immigrant Girls (n=843)</b></p> <p>None (ref) vs ≥ 1/d: 1.08 (0.86, 1.35)</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b></p> <p>Breastfeeding, birth weight, siblings, sleep issues, foreign language spoken at home, maternal partnership status</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>46% attrition without information on non-completers</li> <li>Unclear exposure definition</li> <li>Exposure data collection tool not validated</li> <li>Unclear if % missing data was equal across exposure groups</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b></p> <p>No funding was received for this research</p>

**Table 15. Risk of bias for randomized controlled trials examining SSB consumption versus different amount or water consumption and growth, size, body composition and risk of overweight and obesity in children<sup>xxxv, xxxvi</sup>**

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Chen, 2019 <sup>95</sup>	Low	Some Concerns	Some Concerns	Low	Some Concerns
Ebbeling, 2012 <sup>101</sup>	Some Concerns	Low	Low	Low	Some Concerns

<sup>xxxv</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xxxvi</sup> Possible ratings of low, some concerns, or high determined using the "[Cochrane Risk-of-bias 2.0 \(RoB 2.0\)](#) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). *Cochrane Methods. Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). [dx.doi.org/10.1002/14651858.CD201601](https://doi.org/10.1002/14651858.CD201601).)



**Table 16. Risk of bias for the non-randomized controlled trial examining SSB consumption versus different amount or water consumption and growth, size, body composition and risk of overweight and obesity in children<sup>xxxvii, xxxviii</sup>**

	Confounding	Selection of participants	Classification of interventions	Deviations from intended interventions	Missing data	Outcome measurement	Selection of the reported result
Altman, 2015 <sup>83</sup>	Moderate	Low	Low	Low	Low	Low	Moderate

<sup>xxxvii</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xxxviii</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the “[Risk of Bias in Non-randomized Studies of Interventions \(ROBINS-I\) tool](#)” (Sterne JAC, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JPT. ROBINS-I: a tool for assessing risk of bias in non-randomized studies of interventions. *BMJ* 2016; 355; i4919; doi: 10.1136/bmj.i4919.)

**Table 17. Risk of bias for prospective cohort studies examining SSB consumption versus different amount or water consumption and growth, size, body composition and risk of overweight and obesity in children<sup>xxxix, xl</sup>**

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Alviso-Orellana, 2018 <sup>84</sup>	Serious	Low	Serious	Moderate	Low	Moderate	Moderate
Ambrosini, 2013 <sup>85</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Bigornia, 2015 <sup>89</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Cantoral, 2016 <sup>93</sup>	Serious	Low	Low	Low	Low	Low	Moderate
Carlson, 2012 <sup>66</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
DeBoer, 2013 <sup>99</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
De Coen, 2014 <sup>97</sup>	Moderate	Low	Low	Low	Low	Low	Moderate
Dong, 2015 <sup>15</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Dubois, 2016 <sup>17</sup>	Serious	Low	Low	Low	Moderate	Moderate	Moderate
Durao, 2015 <sup>100</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Enes, 2013 <sup>102</sup>	Serious	Moderate	Low	Low	Moderate	Low	Moderate
Field, 2014 <sup>103</sup>	Serious	Low	Low	Low	Moderate	Serious	Moderate
French, 2012 <sup>105</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Gopinath, 2013 <sup>107</sup>	Moderate	Low	Moderate	Moderate	Moderate	Low	Serious
Guerrero, 2016 <sup>70</sup>	Serious	Low	Serious	Low	Moderate	Low	Moderate
Hasnain, 2014 <sup>27</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Hooley, 2012 <sup>109</sup>	Serious	Low	Moderate	Moderate	No Information	Low	Serious
Jensen, 2013 <sup>110</sup>	Serious	Low	Serious	Low	Low	Low	Serious
Jensen, 2013 <sup>111</sup>	Serious	Low	Moderate	Low	Moderate	Low	Serious

<sup>xxxix</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xl</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

Johnson, 2012 <sup>112</sup>	Serious	Low	Serious	Low	Moderate	Low	Moderate
Laska, 2012 <sup>116</sup>	Moderate	Low	Low	Low	Moderate	Low	Moderate
Lee, 2015 <sup>117</sup>	Moderate	Low	Low	Low	Moderate	Low	Moderate
Macintyre, 2018 <sup>119</sup>	Serious	Low	Serious	Moderate	Moderate	Low	Moderate
Marshall, 2018 <sup>2</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Marshall, 2019 <sup>41</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Millar, 2014 <sup>121</sup>	Serious	Low	Serious	Low	Moderate	Low	Moderate
Mirmiran, 2015 <sup>122</sup>	Serious	Low	Serious	Moderate	Low	Low	Moderate
Muckelbauer, 2016 <sup>123</sup>	Serious	Low	Serious	Low	Low	Low	Moderate
Olsen, 2012 <sup>124</sup>	Serious	Low	Moderate	Moderate	Moderate	Low	Moderate
Seo, 2015 <sup>128</sup>	Serious	Moderate	Serious	Low	No Information	Low	Moderate
Shroff, 2014 <sup>129</sup>	Serious	Low	Moderate	Moderate	Moderate	Low	Moderate
Sichieri, 2013 <sup>130</sup>	Serious	Moderate	Moderate	Moderate	Moderate	Low	Moderate
Stoof, 2013 <sup>132</sup>	Serious	Low	Moderate	Moderate	Moderate	Low	Moderate
Thurber, 2017 <sup>134</sup>	Serious	Low	Serious	Moderate	Low	Low	Moderate
Traub, 2018 <sup>135</sup>	Serious	Moderate	Serious	Low	Moderate	Low	Moderate
Wheaton, 2015 <sup>138</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Whetstone, 2012 <sup>59</sup>	Serious	Critical	Serious	Low	Moderate	Moderate	Serious
Yiotaldiotariotam, 2013 <sup>139</sup>	Serious	Moderate	Low	Low	Moderate	Low	Moderate
Zheng, 2014 <sup>140</sup>	Serious	Low	Low	Low	Low	Low	Moderate
Zheng, 2015 <sup>1</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Zheng, 2015 <sup>62</sup>	Serious	Low	Serious	Moderate	Serious	Low	Moderate
Zheng, 2015 <sup>61</sup>	Serious	Low	Moderate	Moderate	Low	Low	Moderate
Zulfiqar, 2019 <sup>141</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate

**Table 18: Summary of articles examining the relationship between SSB consumption versus different amount or water consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>xli</sup>**

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
CONTROLLED TRIALS			

<sup>xli</sup> Abbreviations: adj: adjusted; ANOVA: analysis of variance; BMI: body mass index; BMIZ: BMI z-score; CI: confidence interval; CTSA: Clinical and Translational Science Awards; d: day(s); DXA or DEXA: dual-energy X-ray absorptiometry; FFQ: food frequency questionnaire; HR: hazard ratio; mo: month(s); NA: not applicable; NCI: National Cancer Institute; NCRR: National Center for Research Resources; NHLBI: National Heart, Lung, and Blood Institute; NIA: National Institute on Aging; NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases; NIH: National Institutes of Health; NR: not reported; NRCT: non-randomized controlled trial; NS: not significant; OR: odds ratio; Q: quintile; RCT: randomized controlled trial; RR: relative risk; SD: standard deviation; SE: standard error; SEM: standard error of the mean; SES: socioeconomic status; SSB: sugar-sweetened beverage; SSSD: sugar sweetened carbonated soft drinks; TEI: total energy intake; unadj: unadjusted; WC: waist circumference; wk: week(s); y: year(s)  
Red font indicates a statistically significant detrimental relationship, and green font indicates a statistically significant beneficial relationship.

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Maersk, 2012<sup>120</sup></b>  <b>RCT, Denmark</b>  Baseline N=60, Analytic N=47 (Attrition: 22%); Power: NR</p> <p><b>Recruitment:</b> NR</p> <p><b>Participant characteristics: adults with overweight and obesity</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 72%</li> <li>• Age: ~39y (Range 20-50y)</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI ~32 kg/m<sup>2</sup> (Range 26-40)</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In overweight adults and those with obesity, drinking sucrose-sweetened cola (1 L/d) compared to water (1 L/d) for 6 months did not significantly affect weight, total fat mass, or lean mass. There was no difference in energy intake between groups during the intervention.</p>	<p><b>Intervention:</b> Sucrose-sweetened soft drink (SSSD; Coca Cola; 1 L/d), n=10</p> <p><b>Comparator:</b> Still mineral water (Aqua d'or; 1 L/d), n=13</p> <p>Other interventions: milk, aspartame-sweetened diet cola</p> <p><u>Intervention duration:</u> 6mo</p> <p><u>Intervention compliance:</u> empty bottles or cartons every 3-4wk; 7-d dietary records at baseline, 3mo, 6mo; compliance NR</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Mean SSSD at baseline: 184 mL/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 6mo follow-up</li> <li>• Weight: method NR</li> <li>• Total fat mass and lean body mass determined by DXA</li> </ul>	<p><b>Weight</b>, kg, ANOVA, Mean (SEM)  <b>Change over time, between groups:</b>  Water: 0.576 (1.0)  SSSD: 1.28 (1.1)</p> <p><b>Total fat mass</b>, kg, ANOVA, Mean (SEM)  <b>Change over time, between groups:</b>  Water: 0.490 (2.6)  SSSD: 3.14 (2.7)</p> <p><b>Lean mass</b>, kg, ANOVA, Mean (SEM)  <b>Change over time, between groups:</b>  Water: -0.189 (0.8)  SSSD: 0.423 (0.8)</p> <p>Data are also provided on <u>subcutaneous abdominal adipose tissue (SAAT)</u>, <u>visceral adipose tissue (VAT)</u>, and <u>the ratio of the two</u>; none were significant for the exposures of interest.</p>	<p><b>TEI adjusted:</b> Yes (Between-group differences NS at baseline or during study)  <b>Change in EI between groups:</b>  Data NR, P=0.3</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, physical activity (NS at baseline)</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Bone mass, blood pressure, metabolic factors (leptin, cholesterol, triglycerides, fasting plasma glucose, fasting plasma insulin, HOMA-IR)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Randomization and allocation methods NR</li> <li>• Baseline imbalances between groups</li> <li>• No power calculation and likely underpowered</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding Sources:</b>  Danish Council for Strategic Research; The Food Study Group/Danish Ministry of Food, Agriculture and Fisheries; Novo Nordic Foundation; Clinical Institute at Aarhus University, Denmark; Danish Dairy Company, Arla Foods</p>

**Partridge, 2016**<sup>126</sup>

**NRCT, 'TXT2BFiT' mHealth intervention, Australia**

Baseline N=125, Analytic N=123; Attrition: 2%; Power: NR

**Recruitment:** primary care and print and electronic media in Greater Sydney Area

**Participant characteristics: young adults at risk of weight gain who consumed >1L SSB/wk**

- Total energy intake: NR
- Sex (female): 59%
- Age: 29% 18-24y, 22% 25-29y, 49% 30-35y
- Race/ethnicity: 67% English, 33% Other
- SES: 93.5% Highest quintiles; 60% ≥University bachelor degree
- Anthropometry: Weight, kg ~79 (12.6); BMI range 23-32
- Physical activity: 6.64 (3.33) d/wk; ~1620 MET min/wk
- Smoking: NR

**Summary of findings:**

A 3-month mHealth intervention in young adults resulted in significant weight loss in the intervention group compared to control. SSB intake was a significant mediator of the intervention effect on weight loss at 3- and 9-months. Specifically, the intervention decreased SSB consumption (~decrease of 500 mL/wk), which significantly mediated the effect on weight at 3- and 9-months, accounting for 7.6 and 17.4 % of the intervention effect on weight change respectively.

**Intervention: SSB intake**

An mHealth intervention consisting of 5 personalized coaching calls with a dietitian, 8 weekly gender and stage-of-change specific text messages targeting fruit and vegetable consumption, take-out meal consumption, SSB consumption and physical activity levels, weekly emails and access to smartphone applications and study website. Maintenance phase lasted 6mo and participants received two booster coaching calls, monthly text messages and emails and had ongoing access to the smartphone applications and website.

**Comparator:** Change in SSB intake, (continuous; svg/d)

Intervention duration: 3mo

Intervention compliance/ diet assessment method and timing:

- At baseline, after 3mo intervention, and after 6mo maintenance
- Validated short questions on usual weekly intake of SSB

**Study beverage intake:**

- Habitual SSB intake ≥1 L/wk

**Outcome assessment methods/timing:**

- At baseline, after 3mo intervention, and after 6mo maintenance
- Weight was self-reported via online survey

**Weight**, kg, Baseline, 3mo, 9mo, Mean (SD)

78.4 (11.2), 76.0 (10.7), 74.9 (10.8)

**Change in weight:** By change in SSB intake, Linear regression,  $\beta$  (SE)

At 3mo: -0.50 (0.27), P=0.07

**At 9mo: -0.61 (0.26), P=0.02**

**TEI adjusted:** No

**Confounders accounted for:**

- Key confounders: sex, anthropometry at baseline
- Other factors considered: N/A

**Confounders NOT accounted for:**

- Key confounders: age, race/ethnicity, SES, physical activity, smoking
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:**

Allocation, general practitioner practice

**Limitations:**

- Not all key confounders accounted for
- No info on amount of missing data/ amount of imputation required
- Weight was self-reported

**Funding Source:**

Hospitals Contribution Fund (HCF)  
Medical Research Foundation;  
Commonwealth Government of Australia

**Tate, 2012<sup>133</sup>**

**RCT, Choose Healthy Options  
Consciously Everyday (CHOICE), US**

Baseline N=318, Analytic N= 272;  
Attrition: 15% (ITT, n=318); Power: With  
100 participants per arm and a set at 0.05,  
we had 90% power to detect a difference  
of 1.8 kg with an SD of 3.4 kg and 25%  
attrition

**Recruitment:** clinic

**Participant characteristics:  
overweight/obese adults who consume  
≥280 kcal/d of caloric bevs**

- Total energy intake: NR
- Sex (female): 84%
- Age: 42 (10.7)y (Range 18-65y)
- Race/ethnicity: 54% black, 40% white, and 6% other
- SES: college graduate or beyond ~55%
- Anthropometrics: BMI ~36.3 (Range 25-49.9)
- Physical activity: NR
- Smoking: 9% current smoker

**Summary of findings:** After a 6-month intervention in overweight and obese adults, there was no significant difference in weight loss, likelihood of achieving 5% weight loss, or waist circumference between participants who were encouraged to substitute water for caloric beverages and those in the "attention control" group. Participants in all groups lost a significant amount of weight.

**Intervention (Water, n=108):** encouraged to replace ≥2 servings (≥200 kcal) per day of caloric beverages with water; could choose any combination of bottled still and nonsweetened sparkling water; provided with beverages at monthly group meetings

**Comparator: "Attention Control" (AC, n=105)** equal treatment contact time and attention, monthly group sessions and weigh-ins, weekly monitoring; AC group given general weight-loss information (eg, instructed to read product labels, increase vegetable consumption, control portions, and increase physical activity); they were not given weight-loss calorie-reduction or physical activity goals. They were not encouraged to change beverage intake (beverages were not mentioned during the lessons or group sessions) and were not provided with beverages.

2<sup>nd</sup> Intervention Group: (Diet bevs, n=105)

Intervention duration: 6 mo  
Intervention compliance: DB and Water groups consumed fewer beverage calories than the control group at 3mo and 6mo

**Study beverage intake (kcal):** 0, 3, 6mo  
**Control:** 329.3 (280.2, 378.4) 216.5 (183.0, 249.9) 222.6 (190.6, 254.7, P<0.0001  
**Water:** 326.6 (286.1, 367.0) 128.6 (102.0, 155.2) 139.2 (112.2, 166.1), P<0.0001;  
Group\*time: P=0.02; Vs. Control: P<0.0001

**Outcome assessment methods/timing:**

- At baseline, 3mo, 6mo
- Weight measured after 12h fast using digital scale
- Height measured using stadiometer at baseline
- Waist circumference measured at the iliac crest

**Weight**, kg, within group, over time: baseline, 3mo, 6mo; mean (95% CI)

**Control:** 102.6 (99.1, 106.1), 101.1 (97.7, 104.6), 100.7 (97.2, 104.2), P<0.0001

**Water:** 98.4 (95.2, 101.6), 97.2 (94.0, 100.4), 96.5 (93.3, 99.7), P<0.0001  
**Between group:** NS

**Likelihood of achieving 5% weight loss:** OR (95% CI)

Control: (ref)

Water: 1.87 (0.84, 4.14), P=0.13

**Waist circumference**, cm, within group, over time: baseline, 3mo, 6mo, mean (95% CI)

**Control:** 116.5 (113.9, 119.2), 116.8 (114.1, 119.5), 115.9 (113.2, 118.7), P=0.0107

**Water:** 115.1 (112.6, 117.6), 114.4 (111.9, 116.9), 113.1 (110.5, 115.8), P=0.0143

**Between group:** NS

**TEI adjusted:** No

**Food Energy Intake, kcal/d over time: baseline, 3mo, 6mo, mean (95% CI)**

**Control:** 1861.6 (1703.8, 2019.4), 1501.5 (1391.4, 1611.5), 1386.9 (1287.2, 1486.6), P<0.0001

**Diet bevs:** 1886.9 (1752.1, 2021.8), 1621.3 (1512.0, 1730.7), 1487.6 (1382.7, 1592.5), P<0.0001; Vs. control: P<0.0001

**Water:** 1715.5 (1605.9, 1825.1), 1396.9 (1317.6, 1476.2), 1371.1 (1253.4, 1488.7), P<0.0001; Vs. Control: P<0.0001

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking
- Other factors considered: medications

**Confounders NOT accounted for:**

- Key confounders: N/A
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, supplements, alcohol

**Additional model adjustments:** N/A

**Limitations:**

- Amount of carbonated and/or caffeinated versions of beverages was not taken into account
- Trial registry did not include data analysis plan

**Funding Source:**

Nestle Waters USA

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Vazquez-Duran, 2016<sup>137</sup></b>  <b>RCT, Clinical Trial, Mexico</b>            Baseline N=148, Analytic N=146 (Attrition: 1%); Power: a sample size of 31, which was increased by 20% loss to follow up, gave a total of 37 patients in each group. <math>\alpha=0.05</math>, <math>\beta=80\%</math> to detect -1.6% change in BMI in intervention group with SD 0.8</p> <p><b>Recruitment:</b> María Elena Maza Brito School of Nursing in Mexico City</p> <p><b>Participant characteristics: young adults consuming <math>\geq 12</math> oz/d SSB</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 81%</li> <li>• Age: 21.99 (0.25) y</li> <li>• Race/ethnicity: NR</li> <li>• SES: all nursing students</li> <li>• Anthropometrics: BMI: 26.24 (0.36) kg/m<sup>2</sup>; Overweight: 45%; Obesity: 16%</li> <li>• Physical activity: &lt;1hr/d of vigorous physical activity (inclusion criteria)</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            In young adults with habitual SSB intake <math>\geq 12</math> oz/d, drinking their usual consumption of caloric and non-caloric beverages compared to participants who drank no SSB for 6 mo resulted in greater increases in BMI, waist circumference, hip circumference, and phase angle (measure of body composition). There was no association with resistance/height (also a measure of composition).</p>	<p><b>Intervention:</b> No sweetened beverages permitted (only plain water, lemon and hibiscus flavored water, coffee and tea without sugar), n=49</p> <p><b>Comparator:</b> Usual intake, n=49</p> <p>Other interventions: (2<sup>nd</sup> intervention group) Only beverages with non-caloric sweeteners allowed (including plain water, lemon and hibiscus flavored water, coffee and tea without sugar), n=50</p> <p><u>Intervention duration:</u> 6mo</p> <p><u>Intervention compliance:</u> 24hr food record 1x/week for full 6-month intervention</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Habitual SSB intake: <math>\geq 12</math> oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 3mo and 6mo follow-up</li> <li>• Weight and height measured according to anthropometric standardization reference manual</li> <li>• Body composition (resistance/height and phase angle) evaluated by bioelectric impedance analysis</li> <li>• Waist, hip, and arm circumferences evaluated according to the anthropometric reference manual</li> </ul>	<p>All Linear regression, Mean (SD)  <b>BMI % of change</b>  <b>Change over time, within group:</b> 3mo, 6mo            No SSB: -1.75 (0.6), -3.34 (0.75)            SSB (Control): 0.54 (0.06), 0.57 (0.07)  <b>Change over time, between groups:</b> 6mo  <b>P&lt;0.001</b></p> <p><b>Waist Circumference % of change</b>  <b>Change over time, within group:</b> 3mo, 6mo            No SSB: -2.45 (0.44), -4.07 (0.54)            SSB (Control): 0.53 (0.16), 0.62 (0.60)  <b>Change over time, between groups:</b> 6mo  <b>P&lt;0.001</b></p> <p><b>Hip Circumference % of change</b>  <b>Change over time, within group:</b> 3mo, 6mo            No SSB: -1.63 (0.30), -3.00 (0.44)            SSB (Control): 0.33 (0.27), 0.51 (0.31)  <b>Change over time, between groups:</b> 6mo  <b>P&lt;0.001</b></p> <p><b>Resistance/Height % of change</b>  <b>Change over time, within group:</b> 3mo, 6mo            No SSB: -1.92 (1.61), -2.12 (0.95)            SSB (Control): -0.43 (1.83), 0.34 (0.62)  <b>Change over time, between groups:</b> 6mo  <b>P=0.02</b></p> <p><b>Phase angle % of change</b>  <b>Change over time, within group:</b> 3mo, 6mo            No SSB: 4.88 (0.76), 8.40 (0.85)            SSB (Control): 3.02 (0.70), 3.58 (0.96)  <b>Change over time, between groups:</b> 6mo  <b>P&lt;0.005</b></p>	<p><b>TEI adjusted:</b> Yes (all participants were on individualized isocaloric diets)</p> <p><b>Energy Intake, % change from baseline EI, Mean (SD)</b>  <b>EI, change over 6mo within group:</b>            No SSB: -16.88 (2068)            Control: -6.92 (3.46)  <b>Change over time, between groups:</b>            P=0.01</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: (No baseline differences) sex, age, anthropometry at baseline</li> <li>• Other factors considered: total energy intake, medications</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES, physical activity, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> </ul> <p><b>Funding Sources:</b>            Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<b>PROSPECTIVE COHORT STUDIES</b>			
<p><b>Appelhans, 2017<sup>86</sup></b>  <b>Prospective Cohort Study, Study of Women's Health Across the Nation (SWAN), US</b>  Baseline N=2870, Analytic N=1448; Attrition: 50%; Power: NR</p> <p><b>Recruitment:</b> recruited from five ethnic/racial groups: African American (Boston, MA; Chicago, IL; Detroit, MI, area; and Pittsburgh, PA); Chinese (Oakland, CA, area); Hispanic (Newark, NJ); Japanese (Los Angeles, CA); and non-Hispanic white (all sites)</p> <p><b>Participant characteristics: middle-aged women</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~1831 kcal/d</li> <li>• Sex (female): 100%</li> <li>• Age: ~46y</li> <li>• Race/ethnicity: 51% Non-Hispanic White, 25% African American, 24% Chinese/Japanese</li> <li>• SES: &lt;\$35K: 23%; &gt;\$75K: 33.8%</li> <li>• Anthropometrics:</li> <li>• Physical activity: 7.9 (scores range from 3 to 15 and higher score representing more frequent engagement in physical activity)</li> <li>• Smoking: 12.4% Current smoker</li> </ul> <p><b>Summary of findings:</b>  There was a positive association between intake of energy-dense, nonalcoholic beverages and odds of developing abdominal obesity across 14y follow-up (i.e., greater intake was associated with odds of abdominal obesity increasing at a faster rate).</p>	<p><b>Exposure of interest:</b> Energy-dense, nonalcoholic beverages (includes Kool-aid, Hi-C, or other drinks with added vitamin C; Snapple, Calistoga, or sweetened bottled waters or iced teas; regular cola soft drinks; coffee or tea consumed with condiments that collectively yield an energy density <math>\geq 0.165</math> kcal/g); 1 svg=355 mL, 12 oz</p> <p><b>Comparators:</b> Energy-dense, nonalcoholic beverages intake, continuous</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated SWAN FFQ; interviewer-administered; assesses the usual frequency and portion sizes</li> <li>• At baseline, 5y, 9y</li> </ul> <p><b>Study beverage intake:</b> 355mL/d; Mean (SD)</p> <ul style="list-style-type: none"> <li>• Energy-dense, nonalcoholic beverages: 0.58 (1.01)</li> <li>• Low-calorie teas, coffee, and diet cola: 1.10 (1.31)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, annually up to 14y (mean follow-up ~13y)</li> <li>• Waist circumference was measured to the nearest 0.1 cm with a measuring tape placed horizontally around the participant at the narrowest part of the torso</li> <li>• Abdominal obesity: Waist circumference <math>\geq 80</math>cm for Chinese/Japanese women and <math>\geq 88</math>cm for other ethnic/racial groups</li> </ul>	<p><b>Incident Abdominal Obesity</b>, across 14y follow-up, OR (95% CI)  Intake: 0.66 (0.41, 1.06)  <b>Time*intake: 1.10 (1.03, 1.16)</b></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: anthropometry at baseline</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Study site, menopausal status, hormone therapy use, depressive symptoms</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Length of follow-up may not be consistent for all participants</li> <li>• No information on non-completers</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Auerbach, 2018<sup>64</sup></b>  <b>Prospective Cohort Study, Women's Health Initiative, United States</b>  Baseline N=122970, Analytic N=49106 (Attrition: 60.1%); Power: NR</p> <p><b>Recruitment:</b> clinical centers in 24 states</p> <p><b>Participant characteristics: postmenopausal women</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d, Mean (SD): 1636 (620)</li> <li>Sex (female): 100%</li> <li>Age: 57.9 (4.1) y</li> <li>Race/ethnicity: White 84%, African American 7.6%, Hispanic/Latino 4.0%, Asian/Pacific 3.0%</li> <li>SES: College degree or higher 48%, Annual household income ≥ \$75,000 15.4%</li> <li>Anthropometrics: Mean (SD), BMI= 26.2 (4.0) kg/m<sup>2</sup></li> <li>Physical activity: Recreational physical activity level (MET-hours/wk): 4.3 (3.9)</li> <li>Smoking: Current smoking 7.1%</li> </ul> <p><b>Summary of findings:</b>  In postmenopausal women, SSB intake was significantly associated with increased weight over 3 years.</p>	<p><b>Exposure of interest:</b> SSB intake (1 svg = 6 oz)</p> <p><b>Comparator:</b> SSB intake (continuous; svg/d)</p> <p>Other exposure measures: 100% fruit juice</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents usual intake</li> <li>At baseline, 3y follow-up</li> </ul> <p><b>Study beverage intake:</b> svg/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>SSB intake: 0.30 (0.54)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 3y follow-up</li> <li>Weight measured using standardized protocol and calibrated scales</li> </ul>	<p><b>Weight, lb/3-year change per svg/d increase</b>, Linear mixed effects model, B (95% CI):  <b>TEI unadj: 0.58 (0.26, 0.90)</b>  <b>TEI adj: 0.36 (0.29, 0.69)</b></p> <p><b>Analysis with Multiple Imputation (n=74,397)</b>  <b>TEI unadj: 0.58 (0.31, 0.85)</b>  <b>TEI adj: 0.36 (0.34, 0.64)</b></p> <p><b>Stratified by BMI group</b>  BMI 18.5-24.9 (n=20,494):  TEI unadj: 0.63 (-0.04, 1.29)  TEI adj: 0.51 (-0.17, 1.18)</p> <p>BMI 25.0-29.9 (n=18,543):  <b>TEI unadj: 0.49 (0.06, 0.92)</b>  TEI adj: 0.29 (-0.15, 0.73)</p> <p>BMI 30.0-34.9 (n=9,588):  TEI unadj: 0.56 (-0.05, 1.18)  TEI adj: 0.21 (-0.41, 0.83)</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: N/A</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Hormone replacement therapy status, 3-year change in healthy eating index diet quality score</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NHLBI; NIH</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Barone-Gibbs, 2012<sup>87</sup></b></p> <p><b>Prospective Cohort Study, secondary analysis from RCT (WOMAN: Women on the Move through Activity and Nutrition; control group only), United States</b></p> <p>Baseline N= 240, Analytic N=216; Attrition: 10%; Power: NR</p> <p><b>Recruitment:</b> via direct mailings from selected ZIP codes in Allegheny County, Pennsylvania, starting in 2002</p> <p><b>Participant characteristics: ovwt or obese postmenopausal women enrolled in a diet and physical activity lifestyle intervention but only data from control group</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 100%</li> <li>• Age: ~57y (52-62y)</li> <li>• Race/ethnicity: 87% White</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI ~31 (25-40); ~82 kg; WC&gt;80cm</li> <li>• Physical activity: ~12 MET-h/wk</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In overweight or obese postmenopausal women, higher SSB intake was associated with higher weight at 48 months but not at 6 months.</p>	<p><b>Exposure of interest:</b> SSB intake</p> <p><b>Comparators:</b> SSB intake (continuous, 12-oz svg/d)</p> <p>Data reported from women randomized to control group; offered 6 seminars during the first year and 2-4 yearly during years 2-4; Seminars focused on general women's health (e.g., smoking cessation, health benefits of physical activity), but not specifically weight loss</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated questionnaire assessing regular eating behaviors in the past month</li> <li>• At baseline, 6mo, 48mo</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• SSB: 0-1 12oz svg/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 6mo, 48mo</li> <li>• Weight (Methods NR)</li> </ul>	<p><u><b>Change in weight at 6 mo (n=227).</b></u></p> <p>Linear regression, <math>\beta = 0.57</math>, <math>P = 0.120</math></p> <p><u><b>Change in weight at 48 mo (n=216).</b></u></p> <p>Linear regression, <b><math>\beta = 1.28</math>, <math>P = 0.23</math></b></p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, anthropometry at baseline, physical activity (at 48mo not 6mo)</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, race/ethnicity, SES, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Outcome assessment methods NR</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>NHLBI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Barrio-Lopez, 2013<sup>88</sup></b>  <b>Prospective Cohort Study, Seguimiento Universidad de Navarra (SUN) Project, Spain</b>  Baseline N=9849, Analytic N= 8157; Attrition: 17%; Power: NR</p> <p><b>Recruitment:</b> all university graduates who are contacted and followed using mailed or Web-based questionnaires</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: ~9929 kJ/d</li> <li>Sex (female): ~65%</li> <li>Age: ~36y</li> <li>Race/ethnicity: NR</li> <li>SES: "restricted cohort to highly educated participants"</li> <li>Anthropometrics: BMI~22.7 kg/m<sup>2</sup></li> <li>Physical activity: Leisure-time physical activity ~20.0 MET-hr/wk</li> <li>Smoking: ~24% Current smokers, ~26% Former smokers</li> </ul> <p><b>Summary of findings:</b>  Higher SSB intake is associated with increased weight and greater odds of central obesity over a 6-8y follow-up.</p>	<p><b>Exposure of interest:</b> SSB (sugar-sweetened carbonated colas and fruit-flavored carbonated sugar soft drinks; Not including artificially sweetened beverages, bottled fruit juice)</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Baseline SSB intake, categorical; quintiles</li> <li>Change in SSB intake, categorical; quintiles <ul style="list-style-type: none"> <li>Quintile 1: those who decreased most of their consumption (ref)</li> <li>Quintile 5 for those participants who increased most of their consumption</li> </ul> </li> </ul> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Validated semi-quantitative FFQ; frequency of SSB over past year</li> <li>At baseline, 6y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSB: 4.9% consumed ≥1 svg/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At 6y and 8y follow-up</li> <li>Self-reported waist circumference (WC); measuring tape was provided with explanation about how to measure their own waist</li> <li>Weight change: assessment methods NR</li> </ul>	<p><b>Odds of elevated waist circumference (≥94 cm in males, ≥80 cm in females) by change in SSB; OR (95% CI)</b>  Q1: ref  <b>Q2: 1.3 (1.1, 1.6)</b>  Q3: 1.2 (1.0, 1.4)  <b>Q4: 2.1 (1.8, 2.6)</b>  <b>Q5: 2.3 (1.9, 2.7)</b>  <b>P for trend&lt;0.001</b></p> <p><b>Association between weight change (kg) and change in SSB; β (95% CI)</b>  Q1: ref  <b>Q2: 0.5 (0.2, 0.9)</b>  <b>Q3: 0.5 (0.2, 0.8)</b>  <b>Q4: 1.1 (0.8, 1.4)</b>  <b>Q5: 1.3 (1.1, 1.6)</b>  <b>P for trend&lt;0.001</b></p> <p><b>Association between Baseline SSB (quintile) and elevated waist circumference; OR (95%CI):</b>  <b>Q1 (ref) vs Q5: 1.8 (1.01, 1.37)</b>  Other comparisons NR</p>	<p>TEI adjusted: Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Consumption of red meat, French fries, fast food consumption and adherence to the Mediterranean dietary pattern</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Waist circumference self-reported</li> <li>Weight assessment methods NR</li> <li>No preregistered data analysis plan</li> <li>Low SSB consumption</li> </ul> <p><b>Funding sources:</b>  Spanish Government; Navarra Regional Government; University of Navarra</p>

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<p><b>Boggs, 2013<sup>90</sup></b>  <b>Prospective Cohort Study, Black Women's Health Study (BWHS), United States</b>            Baseline N=22879, Analytic N=19479; Attrition: 15%; Power: NR</p> <p><b>Recruitment:</b> African American women from across the U.S. were enrolled through mailed health questionnaires</p> <p><b>Participant characteristics: African American women</b></p> <ul style="list-style-type: none"> <li>Total energy intake:</li> <li>Sex (female): 100%</li> <li>Age: ~31y (21-39y)</li> <li>Race/ethnicity: 100% African American</li> <li>SES: education ≥16y: ~50%</li> <li>Anthropometrics: BMI: ~24 (18.5-29.9)</li> <li>Physical activity: vigorous ≥5hr/wk ~18%</li> <li>Smoking: Current smoker ~13%</li> </ul> <p><b>Summary of findings:</b>            In African American women, SSB intake is not significantly associated with incident obesity. When stratified by baseline age and BMI, in women 21-29 years old and with a BMI between 18.5-24.9 at baseline, drinking 1 SSB/month compared to 1 SSB/day was associated with greater incident obesity than drinking &lt;1 SSB/month.</p>	<p><b>Exposure of interest:</b> Regular soft drinks (not diet soda)</p> <p><b>Comparators:</b> SSB, categorical:</p> <ul style="list-style-type: none"> <li>&lt;1 drink/mo (ref)</li> <li>1-7/mo</li> <li>2-6/wk</li> <li>1/d</li> <li>≥2/d</li> </ul> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Validated FFQ (self-administered modified version of the Block-National Cancer Institute FFQ); specified frequency and portions</li> <li>At baseline (1995), 6y (2001)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Sugar-sweetened soft drink: ≥1/d: 16%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (1995), every 2y up to 14y (2009)</li> <li>Height and weight: self-report by questionnaire</li> <li>BMI calculated</li> <li>Obesity: BMI≥30 kg/m<sup>2</sup></li> </ul>	<p><b>SSB intake and Incident obesity</b>, HR (95%CI)</p> <p>&lt;1 drink/mo (ref)</p> <p>1-7/mo: 1.05 (0.98, 1.12)</p> <p>2-6/wk: 1.03 (0.95, 1.11)</p> <p>1/d: 1.08 (0.98, 1.20)</p> <p>≥2/d: 1.12 (1.00, 1.25), P-trend= 0.07</p> <p>Stratified by baseline age and BMI; HR (95%CI):</p> <p><b>Baseline age 21-29y &amp; Baseline BMI 18.5-24.9:</b></p> <p>&lt;1 drink/mo (ref)</p> <p><b>1-7/mo: 1.29 (1.07, 1.56)</b></p> <p><b>2-6/wk: 1.40 (1.14, 1.73)</b></p> <p><b>1/d: 1.45 (1.10, 1.92)</b></p> <p>≥2/d: 1.32 (0.96, 1.83), <b>P-trend= 0.01</b></p> <p><b>Baseline age 21-29y &amp; Baseline BMI 25.0-29.9:</b></p> <p>&lt;1 drink/mo (ref)</p> <p>1-7/mo: 0.98 (0.86, 1.12)</p> <p>2-6/wk: 0.98 (0.84, 1.13)</p> <p>1/d: 1.08 (0.89, 1.31)</p> <p>≥2/d: 1.14 (0.93, 1.40), P-trend= 0.19</p> <p><b>Baseline age 30-39y &amp; Baseline BMI 18.5-24.9:</b></p> <p>&lt;1 drink/mo (ref)</p> <p>1-7/mo: 0.95 (0.80, 1.13)</p> <p>2-6/wk: 0.97 (0.80, 1.19)</p> <p>1/d: 0.80 (0.59, 1.10)</p> <p>≥2/d: 1.06 (0.75, 1.50), P-trend= 0.68</p> <p><b>Baseline age 30-39y &amp; Baseline BMI 25.0-29.9:</b></p> <p>&lt;1 drink/mo (ref)</p> <p>1-7/mo: 1.03 (0.93, 1.13)</p> <p>2-6/wk: 0.96 (0.86, 1.07)</p> <p>1/d: 1.03 (0.89, 1.19)</p> <p>≥2/d: 1.02 (0.87, 1.20), P-trend= 0.99</p>	<p><b>TEI adjusted:</b> No, but adjusted for dietary pattern</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: N/A</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>            Parity, geographical region, prudent and Western dietary patterns (quintiles), restaurant burgers</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Weight and height self-reported</li> <li>Length of follow-up differed among participants</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>            Aetna Foundation; NCI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Bundrick, 2014<sup>91</sup></b>  <b>Prospective Cohort Study, Obesity and Diabetes Clinical Research Section (NIDDK), United States</b>  Baseline N= 203, Analytic N= 85; Attrition: 58%; Power: NR  <b>Recruitment:</b> These were participants in other studies at the research unit and are a convenience sample that allowed for the gathering of follow-up information.</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~4400 kcal/d</li> <li>• Sex (female): 37%</li> <li>• Age: 34.3 (8.9)</li> <li>• Race/ethnicity: 64% Native American, 28% White</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI 32.5 (7.4) kg/m<sup>2</sup>; Body fat 31.6 (8.6)%</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Energy from soda intake was associated with greater weight gain over time. Energy from soda and fruit juice combined was not significantly associated with weight change over time.</p>	<p><b>Exposure of interest 1:</b> Soda intake  <b>Exposure of interest 2:</b> SSBs (includes energy from soda and juice)</p> <p><b>Comparators:</b> kcal, continuous</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• After admission to research unit, subjects were fed a weight-maintaining diet for 3 days consisting of 20% of energy from protein, 30% from fat, and 50% from carbohydrate. During final 3 days of admission, subjects were asked to self-select food from a computer-operated vending machine. Water, coffee, 2% milk, orange juice, apple juice, and six 12-oz cans of the subject's soda choice were available each day. Subjects were allowed free access to vending machine and asked to mirror their usual eating behaviors. They were instructed to eat alone and in the vending room, which contained a microwave for any necessary food preparation. They were told to return all wrappers and uneaten food to the vending machine for weighing.</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b> kcal/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>• Soda intake: 379 (252)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, follow-up (Mean 2.5±2.1y; range 6mo to 9.9y)</li> <li>• Height was measured to the nearest centimeter using a stadiometer</li> <li>• Weight was measured using a calibrated digital scale</li> <li>• Body composition measured by dual-energy x-ray absorptiometry (DXA)</li> </ul>	<p><b>Weight change</b>, kg, Spearman correlation  <b>Soda energy (n=85): 0.21, P=0.04</b>  <b>SSB energy (n=59): 0.23, P=0.08</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, anthropometry at baseline</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Follow-up time</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Exposure data only measured at baseline</li> <li>• Differences in energy from soda and SSBs between completers and non-completers</li> <li>• Registry does not include data analysis plan; did not report results for BMI or body composition despite methods reporting these measures</li> </ul> <p><b>Funding source:</b>  NIDDK</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Carroll, 2018<sup>94</sup></b>  <b>Prospective Cohort Study, Place and Metabolic Syndrome (PAMS) Project, Australia</b>  Baseline N=4056, Analytic N=1630;  Attrition: 60%; Power: NR</p> <p><b>Recruitment:</b> randomly selected from the North West Adelaide Health Study (NWAHS), a population-based biomedical cohort of randomly selected adults</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 51%</li> <li>• Age: ~51y</li> <li>• Race/ethnicity: NR</li> <li>• SES: 13% University graduate</li> <li>• Anthropometrics: ~25</li> <li>• Physical activity: NR</li> <li>• Smoking: current smoker 18%</li> </ul> <p><b>Summary of findings:</b> In adults, consuming sugary drinks compared to rarely or never consuming sugary drinks was significantly associated with a ~10yr increase in BMI.</p>	<p><b>Exposure of interest:</b> Sugary drink intake (soft drink, cordial or sports drinks)</p> <p><b>Comparators:</b> Sugary drink intake (categorical; frequency/wk)</p> <ul style="list-style-type: none"> <li>• Rarely/never (0/wk)</li> <li>• &gt;1/wk</li> </ul> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Weekly frequency of sugary drink consumption using Computer-Assisted Telephone Interviews (CATI); not validated</li> <li>• 2007</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Drinks sugary drinks: ~55%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline (2001), and ~8y follow-up (2005-06, 2008-10)</li> <li>• Height measured a wall-mounted stadiometer</li> <li>• Weight measured using standard digital scales</li> <li>• BMI calculated as kg/m<sup>2</sup></li> </ul>	<p><b>Change in BMI.</b> SEM, <math>\beta</math> (95% CI)  <b>0/wk (ref) vs</b>  <b>&gt;0/wk: 0.044 (0.011, 0.077), P=0.009</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, SES, anthropometry at baseline, smoking</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, physical activity</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Marital status</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Exposure data only measured at one time</li> <li>• Exposure is based on frequency, not amount consumed</li> <li>• Exposure data collection tool not validated</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  National Health and Medical Research Council</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Cleland, 2018<sup>96</sup></b></p> <p><b>Prospective Cohort Study, Childhood Determinants of Adult Health study H1 (2004-06) and H2 (2009-10), Australia</b> Baseline N=3049, Analytic N= 1068; Attrition: 65%; Power: NR</p> <p><b>Recruitment:</b> participants from the 1985 Australian Schools Health and Fitness Survey (ASHFS)</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): NR</li> <li>• Age: 31.5 (2.6) y</li> <li>• Race/ethnicity: NR</li> <li>• SES: ~55% university degree</li> <li>• Anthropometrics: BMI ~25 kg/m<sup>2</sup>; Weight Status: 56% Healthy, 31% Overweight, 13% Obese</li> <li>• Physical activity: ~101 mins/wk</li> <li>• Smoking: 81% non-smoker</li> </ul> <p><b>Summary of findings:</b> In adults, there was not a significant association between change in TV-related soft drink consumption and change in BMI over 5 years.</p>	<p><b>Exposure of interest:</b> TV-related soft drink intake</p> <p><b>Comparators:</b> TV-related soft drink intake (categorical; cups/d):</p> <ul style="list-style-type: none"> <li>• No change</li> <li>• Increase</li> <li>• Decrease</li> </ul> <p>Other exposure measures: N/A</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Reported how often they consumed a soft drink (frequency, not amount); no validated</li> <li>• At baseline (2004-06), follow-up (2009-11)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• TV-related soft drink intake: None: ~48%; ≥5 times/wk: ~9%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline (2004-06), follow-up (2009-11)</li> <li>• At baseline, height and weight measured (methods NR)</li> <li>• At follow-up, height and weight self-reported</li> <li>• Healthy: BMI &lt; 25 kg/m<sup>2</sup></li> <li>• Overweight: BMI 25 kg–29.9 kg/m<sup>2</sup></li> <li>• Obese: BMI ≥30 kg/m<sup>2</sup></li> </ul>	<p><b>Change in BMI</b> based on change in TV-related soft drink consumption; ANOVA, Mean (SD)</p> <ul style="list-style-type: none"> <li>○ No change: 0.59 (2.32)</li> <li>○ Increase: 0.90 (2.54)</li> <li>○ Decrease: 0.60 (2.50)</li> </ul> <p>P=0.32</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: anthropometry at baseline</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Exposure data limited to “TV viewing”</li> <li>• Exposure based on frequency of consumption, not amount</li> <li>• No info on non-completers</li> <li>• Follow-up weight and height self-reported</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b> National Health and Medical Research Council, the National Heart Foundation, the Tasmanian Community Fund and Veolia Environmental Services; study sponsors: Sanitarium, ASICS and Target</p>



**Ferreira-Pêgo, 2016<sup>68</sup>**

**Prospective analyses of RCT,  
PREDIMED (PREvención con Dieta  
MEDiterránea), Spain**

Baseline N= 2094; Analytic N=1,868;  
Attrition: 11%; Power: NR

**Recruitment:** participants were selected from all of the PREDIMED recruitment centers with biochemical determinations available for a follow-up of  $\geq 2$  y; all participants were at high risk of CVD due to the presence of T2D or  $\geq 3$  risk factors: current smoking, hypertension, high LDL cholesterol, low HDL cholesterol, overweight or obese, or family history of premature CVD but did not have MetSyn

**Participant characteristics: adults, high risk for CVD**

- Total energy intake, kcal/d, Mean (SD): 2322.6 (~530)
- Sex (female): 52.5%
- Age: ~67y (~6y)
- Race/ethnicity: NR
- SES: NR
- Anthropometrics: BMI: 28.3 (~3.5)
- Physical activity: Leisure time MET-min/d: ~274 (252)
- Smoking: ~58%: Never; ~17% Current; ~26% Former

**Summary of findings:**

In a sample of older adults at high-risk for CVD, consumption of SSBs was not significantly associated with risk of abdominal obesity over a follow-up period of  $\geq 2$ y. Consumption of bottled fruit juices (juice with added sugar or not) was not related to risk of abdominal obesity.

**Exposure of interest:**

- SSBs (1svg=200mL)
- Bottled fruit juices (natural fruit juice that has been chemically changed by using authorized methods and packed and commercialized for subsequent consumption; contains added sugars or not; i.e., contains added sugars or not); (1svg=200mL)

**Comparators:** SSBs, categorical

- <1 serv/wk (Ref)
- 1-5 serv/wk
- >5 serv/wk

Other exposures measured: Natural fruit juices, LNCsBs

**Exposure assessment method and timing:**

- Validated FFQ assessing habitual intake for previous year
- At baseline, annually

**Study beverage intake:**

During follow up: Mean

- SSBs: 14.5 mL/d
- Bottled fruit juices: 16.6 mL/d

**Outcome assessment methods/timing:**

- Baseline, yearly during follow-up period of  $\geq 2$ y
- Weight: measured by trained personnel with calibrated scales
- Height: measured by trained personnel with a wall-mounted stadiometer.
- Waist circumference measured using an anthropometric tape midway between the lower rib and the superior border of the iliac crest
- Abdominal obesity: waist circumference  $\geq 88$ cm in women and  $\geq 102$  cm in men

**Abdominal obesity**, Multivariable time-dependent Cox proportional regression, HR (95% CI)

**SSBs:**

<1 serv/wk: Ref  
1-5 serv/wk: 1.13 (0.81, 1.57)  
>5 serv/wk: 1.20 (0.62, 2.30)  
P for trend: 0.42

**Bottled fruit juices:**

<1 serv/wk: Ref  
1-5 serv/wk: 0.96 (0.72, 1.29)  
>5 serv/wk: 0.46 (0.21, 1.03)  
P for trend: 0.08

**TEI adjusted:** Yes

**Confounders accounted for:**

- Key confounders: sex, age, anthropometry at baseline, physical activity, smoking
- Other factors considered: total energy intake, alcohol (overall alcohol intake & alcohol squared in grams per day)

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity, SES
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements,

**Additional model adjustments:**

Intervention group, average consumption during the follow-up of dietary variables as continuous variables, prevalence of MetS components at baseline

**Limitations:**

- Not all key confounders accounted for
- No information on whether or not amount of missing data varied across exposure groups
- Follow-up time differs among participants
- No preregistered data analysis plan

**Funding sources:**

Spanish Ministry of Health, the Thematic Network, FEDER (European Regional Development Fund), the Centre Català de la Nutrició de l'Institut d'Estudis Catalans, and the Fundació "LaMarat" o de TV3"

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Fowler, 2015</b><sup>104</sup></p> <p><b>Prospective Cohort Study, San Antonio Longitudinal Study of Aging (SALSA), United States</b></p> <p>Baseline N=749, Analytic N=466; Attrition: 38%; Power: NR</p> <p><b>Recruitment:</b> from the San Antonio Heart Study (SAHS) cohort, a community-based prospective study of cardiovascular risk factors among Mexican Americans and European Americans, conducted in San Antonio, Texas, between 1979 and 1996</p> <p><b>Participant characteristics: older adults (65+yo)</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): ~60%</li> <li>• Age: ~69y</li> <li>• Race/ethnicity: ~50% Mexican-American; ~50% European-American</li> <li>• SES: ~35% suburb residents; ~20% barrio residents</li> <li>• Anthropometrics: BMI ~29 kg/m<sup>2</sup>; WC ~100cm; ~78% ovwt/obese</li> <li>• Physical activity: leisure time energy expenditure ~1800 kcal/wk</li> <li>• Smoking: currently smoking ~10%</li> </ul> <p><b>Summary of findings:</b></p> <p>In adults over 65y, there was no association between regular soda intake and waist circumference over time.</p>	<p><b>Exposure of interest:</b> Regular soda intake</p> <p><b>Comparators:</b> Regular soda intake, categorical</p> <ul style="list-style-type: none"> <li>• None/Non-users: 0-0.05 sodas/d</li> <li>• Occasional users: &gt;0 but &lt;1 soda/d</li> <li>• Daily users: ≥1 soda/d</li> </ul> <p>Other exposure measures: diet soda</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Questionnaire; represents weekly intake; non-validated</li> <li>• At baseline and beginning of each follow-up interval (~7y, 8.5, 10y from baseline)</li> </ul> <p><b>Regular soda intake:</b> ~0.25/d</p> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 3 follow-ups: FU1 ~7y, FU2 ~1.5y; FU3 ~1.5y; total ~9.4y (range 4.5-12.5y)</li> <li>• Height and weight measured</li> <li>• BMI calculated as kg/m<sup>2</sup></li> <li>• Waist Circumference (WC) measured in cm at the level of the umbilicus</li> </ul>	<p><b>Change in WC, cm, over interval,</b> By regular soda consumption category, Mean (95% CI)</p> <p>None/Non-User: 1.93 (1.44, 2.42) (ref)</p> <p>Occasional: 0.37 (-0.31, 1.05), P=0.001</p> <p><b>Daily: 1.68 (0.36, 2.99)</b></p> <p>P-trend: NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: N/A</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b></p> <p>Diabetes, length of follow-up interval</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Exposure data collection tool not validated</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>NIA, NIDDK; NCRR; CTSA</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>French, 2012<sup>105</sup></b>  <b>Prospective Cohort Study, from RCT, United States</b></p> <p>Baseline N=NR, Analytic N= 225; Attrition: NR (overall trial attrition: ~9%); Power: among 72 adolescents, a correlation of changes between behavior and BMI z score of .60 of a standard deviation is detectable with 80% power. Among 153 adults, this detectable difference is estimated to be .38</p> <p><b>Recruitment:</b> households recruited from community libraries, worksites, schools, daycare centers, health clinics, religious institutions, park and recreation centers, grocery stores, and food co-ops</p> <p><b>Participant characteristics: households</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): Adolescents 39%; Adults 61%</li> <li>• Age: Adolescents ~15y (Range 12-17y); adults ~41y</li> <li>• Race/ethnicity: ~77% white</li> <li>• SES: Adolescents, ≤\$45K 43%; Adults ≥\$100K 43%</li> <li>• Anthropometrics: Adolescents BMIZ: ~0.71; Adults BMI ~27.2 kg/m<sup>2</sup></li> <li>• Physical activity: adolescents:~105; adults: ~85</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  SSB intake was not significantly associated with 12 month changes in BMI or BMIZ in adults or adolescents, respectively.</p>	<p><b>Exposure of interest:</b> SSBs (fruit drinks, such as cranberry cocktail, Hi-C, lemonade, or Kool-Aid; regular (non-diet) soft drinks, soda, or pop)</p> <p><b>Comparators:</b> categorical: difference between intake at 12mo and baseline, portions/wk</p> <ul style="list-style-type: none"> <li>• Decrease</li> <li>• No change/increase</li> </ul> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Modified FFQ; intake over past month; validation not clear</li> <li>• At baseline and 12mo (after 12mo intervention)</li> </ul> <p><b>Study beverage intake:</b> SSB, portions/wk</p> <ul style="list-style-type: none"> <li>• Adolescents: ~0.28</li> <li>• Adults: ~0.14</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline and 12mo</li> <li>• Height and weight measured by trained research staff</li> <li>• BMI calculated for adults</li> <li>• BMIZ calculated for adolescents</li> <li>• Weight measured using mechanical weight or beam-scale</li> <li>• Age- and sex-specific BMI z-scores (BMIZ) calculated using Lambda-Mu-Sigma method</li> <li>• Obesity (BMI&gt;30 kg/m<sup>2</sup>)</li> </ul>	<p><b>Change in BMIZ/BMI</b> per SSB change over 12mo, LSMean (SE)</p> <p><b>Adolescents (BMIZ)</b></p> <ul style="list-style-type: none"> <li>• Decrease (n= 28): 0.75 (0.08)</li> <li>• No change/increase (n=38): 0.75 (0.07)</li> </ul> <p>P=0.99</p> <p><b>Adults (BMI)</b></p> <ul style="list-style-type: none"> <li>• Decrease (n=78): 29.06 (0.18)</li> <li>• No change/increase (n=68): 29.54 (0.19)</li> </ul> <p>P=0.09</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: adult age, adult race/ethnicity, SES, anthropometry at baseline, smoking</li> <li>• Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, physical activity</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Treatment group, household identification number, baseline SSB intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Attrition can't be determined because baseline n NR</li> <li>• Bias due to missing data can't be determined</li> <li>• Exposure data collection tool validation not clear</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH, NCI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Fresan, 2016<sup>22</sup></b>  <b>Prospective Cohort Study, SUN Cohort, Spain</b>  Baseline N=17,984, Analytic N=15,765 (Attrition: 12%); Power: NR</p> <p><b>Recruitment:</b> Convenience sample of university graduates</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean (SD): ~2342 kcal/d</li> <li>Sex (female): 59.8%</li> <li>Age, Mean (SD): 37.9y (11.7)</li> <li>Race/ethnicity: NR</li> <li>SES: University graduate 100%</li> <li>Anthropometrics, Mean (SD): BMI, 23.49 (3.5)</li> <li>Physical activity, Mean (SD): ~21.7 MET-h/wk</li> <li>Smoking: Current smoker 21.6%, Former smoker 28.4%</li> </ul> <p><b>Summary of findings:</b>  Replacement of sugar sweetened soda beverages with water was associated with decreased incidence of obesity but not significantly associated with 4y weight change in adults.</p>	<p><b>Exposure of interest:</b> SSSBs (sugar-sweetened soda beverages) (1svg = 200mL)</p> <p><b>Comparators:</b> Substituting water for SSSBs (continuous; svg/d water increase/svg/d decrease SSSB)</p> <p>Other exposures: Skim milk, reduced-fat milk, whole milk, milk shakes, regular coffee, decaffeinated coffee, diet soda beverages, fresh orange juice, fresh non-orange juice, bottled juice, water</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Semi-quantitative FFQ previously validated in Spain; Represents intake during previous year</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSSBs: Mean~1.4 svg/wk</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, every 2y</li> <li>BMI from self-reported weight and height</li> <li>Obesity defined as BMI ≥30 kg/m<sup>2</sup></li> </ul>	<p><b>Substitution of 1 svg/d water for 1 svg/d SSSBs, continuous Obesity</b>, OR (95% CI), logistic regression  <b>0.85 (0.75, 0.97)</b>  <b>4y Weight change</b>, g, Mean (95% CI), linear regression  -205 (-425, 16)</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Personal history of obesity, family history of obesity, following a special diet, adherence to Mediterranean dietary pattern, snacking between meals, weight change in past 5y</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Selection into study may have been related to exposure and outcome</li> <li>Weight self-reported</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Spanish Ministry of Health; Navarra Regional Government; University of Navarra</p>

**Funtikova, 2015<sup>23</sup>**

**Prospective Cohort Study, Spain**

Baseline N=3,058 Analytic N=2,112  
(Attrition: 31%) Power: NR

**Recruitment:** Randomly selected population-based sample

**Participant characteristics: adults**

- Total energy intake, Mean: ~11.2 MJ/d kcal/d
- Sex (female): 52.6%
- Age, Mean: ~49.2y
- Race/ethnicity: NR
- SES: Higher education ~37%
- Anthropometrics, Mean: WC, ~89.6 cm
- Physical activity, Mean: ~200 MET-min/d (leisure time)
- Smoking: Current smoker ~26%

**Summary of findings:**

In adults, greater intake of soft drinks was associated with higher WC and odds of developing abdominal obesity.

**Exposure of interest:** Soft drinks (including carbonated sugar-sweetened beverages) (1 svg = 200mL)

**Comparators:**

- Soft drink intake (continuous; 100 kcal/d)
- Soft drink intake (categorical; svg/d)
  - No consumption (ref)
  - <1
  - ≥1
- Soft drink intake (categorical; change in consumption)
  - No consumption (ref)
  - Decrease
  - Increase
  - Maintain

Other exposures: whole milk, skim and low-fat milk, juices

**Exposure assessment method and timing:**

- Validated, 166-item FFQ administered by trained interviewer; Represents intake during previous year
- At baseline, 9y follow-up

**Study beverage intake:**

- Soft drinks, mL/d, Mean (SD): 42 (109); no consumption: 57%, <1 svg/d: 35%, ≥1 svg/d: 8%

**Outcome assessment methods/timing:**

- At baseline, 9y follow-up
- WC measured midway between lowest rib and iliac crest with participant lying horizontally
- Abdominal obesity defined as >102 cm for men and >88 cm for women

**Soft drinks, continuous**

**WC**, cm, Change per 100 kcal/d increase, Mean (95% CI), linear regression::

**1.10 (0.18, 2.03), P=0.018**

**Men:** 0.97 (-0.14, 2.08), P=0.09

**Women:** 1.32 (-0.23, 2.86), P=0.10

**Soft drinks, categorical**

**Abdominal obesity**, OR (95% CI), logistic regression

Incidence by baseline intake:

No consumption (ref)

<1 svg/d: 1.22 (0.90, 1.66)

**≥1 svg/d: 1.77 (1.07, 2.93)**

**Men (n=756)**

No consumption (ref)

<1 svg/d: 1.03 (0.63, 1.69)

≥1 svg/d: 1.62 (0.83, 3.14)

P trend=0.31

**Women (n=723)**

No consumption (ref)

<1 svg/d: 1.39 (0.94, 2.05)

≥1 svg/d: 1.64 (0.74, 3.64)

P trend=0.07

**Soft drinks (change in consumption), categorical**

**WC**, cm, Change by change in consumption, Mean (95% CI), linear regression:

No consumption (ref)

Decrease: 0.49 (-0.61, 1.58), P=0.38

**Increase: 1.50 (0.36, 2.64), P=0.01**

**Maintain: 1.22 (0.13, 2.31), P=0.029**

**Men (n=1000)**

No consumption (ref)

Decrease: 0.90 (-0.58, 2.37), P=0.23

**Increase: 1.52 (0.01, 3.02), P=0.049**

Maintain: 0.03 (-1.41, 1.46), P=0.97

**Women (n=1112)**

No consumption (ref)

Decrease: 0.17 (-1.42, 1.76), P=0.83

Increase: 1.49 (-0.21, 3.18), P=0.09

**Maintain: 2.44 (0.81, 4.06), P=0.003**

**TEI adjusted:** Yes

**Confounders accounted for:**

- Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking
- Other factors considered: total energy intake

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:** Modified Mediterranean diet score, energy under- and over-reporting, dieting (change in consumption models only), other beverage intake

**Limitations:**

- Not all key confounders accounted for
- Attrition 31% without information on non-completers
- No preregistered analysis plan

**Funding sources:**

Catalan Government; Carlos III Health Institute European Fund for Regional Development; Catalonian Agency for the Administration of University and Research Grants

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Gearon, 2018</b><sup>106</sup></p> <p><b>Prospective Cohort Study, Melbourne Collaborative Cohort Study (MCCS), Australia</b></p> <p>Analytic N=7894; Attrition: NR (Attrition in main analyses of cohort was ~35%); Power: NR</p> <p><b>Recruitment:</b> using telephone books and electoral rolls, as well as community announcements and advertisements</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 61%</li> <li>Age: ~46y (Range 27-80y, focused on 40-69y)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI, Women ~25, Men ~26</li> <li>Physical activity: leisure time score ~4</li> <li>Smoking: Never smoker, Women ~62%, Men ~52%</li> </ul> <p><b>Summary of findings:</b></p> <p>There was no significant association between soft drink intake and BMI change 13 years later in women or men.</p>	<p><b>Exposure of interest:</b> Soft drink</p> <p><b>Comparators:</b> categorical</p> <ul style="list-style-type: none"> <li>&lt;1/wk</li> <li>≥ 1/wk</li> </ul> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>FFQ designed for the study; based on frequency, not amount; not validated</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Soda intake:</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline and 13y follow-up</li> <li>Weight and WC measured by practitioner</li> <li>Height measured by practitioner at baseline only</li> </ul>	<p><b>BMI change over 13y</b>, Soft drink &lt;1/wk vs ≥ 1/wk, Linear regression, <math>\beta</math> (95% CI)</p> <p>Women: 0.01 (-0.14, 0.16)</p> <p>Men: -0.02 (-0.14, 0.10)</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: age, smoking</li> <li>Other factors considered: alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, race/ethnicity, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Bias due to missing data can't be determined</li> <li>Exposure data only measured at baseline</li> <li>Exposure classified by frequency not amount</li> <li>Exposure data collection tool not validated</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>NHLBI; NCI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Kaikkonen, 2015<sup>31</sup></b>  <b>Prospective Cohort Study, Young Finns Study, Finland</b>            Baseline N=2276, Analytic N=2170 (Attrition: 25%); Power: NR</p> <p><b>Recruitment:</b> random selection from Finnish national population register</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 53.8%</li> <li>Age: Mean ~32.7y</li> <li>Race/ethnicity: NR</li> <li>SES: Educational status (1=low to 3=high), Mean ~2.11; Occupational status (1=low to 3=high), Mean~1.9</li> <li>Anthropometrics, Mean (SD): BMI (women), 24.38 (0.149); BMI (men), 25.64 (0.138)</li> <li>Physical activity: Leisure-time physical activity (5=low to 15=high), Mean ~9.9</li> <li>Smoking: 23% smoker</li> </ul> <p><b>Summary of findings:</b>            Greater sugar-sweetened soft drink intake frequency was associated with greater increases in BMI among women 24-27y at baseline, but not 30-39y. Sugar-sweetened soft drink intake frequency was not associated with incident obesity in women and was not associated with either change in BMI or incident obesity in men.</p>	<p><b>Exposure of interest:</b> Sugar-sweetened soft drinks</p> <p><b>Comparator:</b> Sugar-sweetened soft drink intake (continuous; portions/mo)</p> <p>Other exposures: milk</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Non-quantitative dietary use frequency questionnaire; Represents habitual intake</li> <li>At baseline (~32.7y)</li> </ul> <p><b>Study beverage intake:</b> Mean (SD)</p> <ul style="list-style-type: none"> <li>Sugar-sweetened soft drink               <ul style="list-style-type: none"> <li>Women: 5.07 (0.23) portions/mo</li> <li>Men: 8.43 (0.29) portions/mo</li> </ul> </li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 6y follow-up</li> <li>Height and weight measured by study personnel</li> <li>Obesity defined as BMI ≥30</li> </ul>	<p><b>BMI</b>, linear regression  <b>Change over time:</b>  <b>Women (n=923):</b>            Not retained in final model; Data NR, P=NS  <b>Women 24-27y (n=265):</b>  <b>Beta=0.147, P=0.013</b>  <b>Women 30-39y (n=658):</b>            Not retained in final model; Data NR, P=NS  <b>Women with weight gain &gt;2kg (n=490):</b>            Not retained in final model; Data NR, P=NS  <b>Men (n=792):</b>            Not retained in final model; Data NR, P=NS  <b>Men 24-27y (n=226):</b>            Not retained in final model; Data NR, P=NS  <b>Men 30-39y (n=566):</b>            Not retained in final model; Data NR, P=NS  <b>Men with weight gain &gt;2kg (n=455):</b>            Not retained in final model; Data NR, P=NS</p> <p><b>Incident obesity</b>, OR (95% CI), logistic regression  <b>Women (n=823):</b>            Not retained in final model; Data NR, P=NS  <b>Men (n=689):</b>            Not retained in final model; Data NR, P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>            Hormones and inflammatory markers, dietary habits and alcohol use, genetic factors, psychological factors, living habits and environment, childhood factors</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Non-quantitative dietary questionnaire not validated</li> <li>Attrition 25% with no information on non-completers</li> <li>No preregistered protocol to compare analyses</li> </ul> <p><b>Funding sources:</b>            Academy of Finland; Social Insurance Institution of Finland; Kuopio, Tampere and Turku University Hospital Medical Funds; Yrjö Jahnsson Foundation; Juho Vainio Foundation; Paavo Nurmi Foundation; Finnish Foundation of Cardiovascular Research; Finnish Cultural Foundation; Sigrid Juselius Foundation; Tampere Tuberculosis Foundation; Emil Aaltonen Foundation; Signe and Ane Gyllenberg Foundation; Bothnia Welfare Coalition for Research and Knowledge</p>

**Kang, 2017<sup>113</sup>**

**Prospective Cohort Study, Korean Genome and Epidemiology Study (KoGES), Korea**

Baseline N=7053, Analytic N=5797  
(Attrition: 18%); Power: NR

**Recruitment:** random sampling of local telephone directory

**Participant characteristics: Korean adults**

- Total energy intake: ~1972 kcal/d
- Sex (female): 48%
- Age: ~51y
- Race/ethnicity: 100% Asian
- SES: 27% Elementary school ( $\leq 6y$ ); 57% Middle/high school (7-12y); 15% College or higher ( $>12y$ )
- Anthropometrics: BMI ~24 kg/m<sup>2</sup>
- Physical activity: ~23.6 MET/d
- Smoking: 56% Non-smokers, 27% Current, 16% Former

**Summary of findings:**

In Korean adults, there was no association between soft drink intake and incidence of abdominal obesity during ~5.7y follow-up.

**Exposure of interest:** Soft drink (carbonated beverages, e.g., Cola and Sprite; did not examine consumption of diet soft drinks)

**Comparators:** Soft drink intake (categorical):

- Rarely/never
- $<1$  svg/wk
- $\geq 1$  svg/wk to  $<4$  svg/wk
- $\geq 4$  svg/wk

Other exposure measures: N/A

**Exposure assessment method and timing:**

- Validated FFQ administered by trained dietitians; represents frequency and portion size of soft drink consumption during the past year
- At baseline (2001-2002), and second follow-up (2005-2006)

**Study beverage intake:**

- Soft drink (svg): 43% rarely/never, 38%  $<1$ /wk, 17%  $\geq 1$ /wk- $<4$ /wk, 3%  $\geq 4$  svg/wk

**Outcome assessment methods/timing:**

- At baseline (2001-2002), and every 2 years over a 10-yr period (Mean 5.7y)
- Height and weight measured with no shoes and while wearing light clothing by trained professionals
- Waist circumference (WC) measured three times then averaged after measuring to the nearest 0.1 cm at narrowest point between lowest rib and the right iliac crest
- Abdominal obesity defined based on MetS criteria from National Cholesterol Education Program Adult Treatment Panel III (WC $\geq 90$ cm for men or  $\geq 80$ cm for women)

**Incidence of Abdominal Obesity,**

Change according to soft drink consumption, Cox proportional hazard, HR (95% CI)

**Total Sample**

Rarely/never (ref) vs.  
 $<1$ /wk: 0.91 (0.81, 1.02)  
 $\geq 1$ /week to  $<4$ /week: 1.11 (0.96, 1.29)  
 $\geq 4$ /week: 1.17 (0.86, 1.60)  
P for trend 0.3434  
P for interaction: 0.5079

**Men**

Rarely/never (ref) vs.  
 $<1$ /wk: 0.87 (0.73, 1.03)  
 $\geq 1$ /week to  $<4$ /week: 1.07 (0.87, 1.31)  
 $\geq 4$ /week: 1.11 (0.74, 1.65)  
P for trend 0.6012

**Women**

Rarely/never (ref) vs.  
 $<1$ /wk: 0.95 (0.81, 1.11)  
 $\geq 1$ /week to  $<4$ /week: 1.12 (0.88, 1.43)  
 $\geq 4$ /week: 1.32 (0.78, 2.23)  
P for trend 0.4387

Results were similar in analysis according to area of residence (rural vs. urban).

**TEI adjusted:** Yes

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking
- Other factors considered: total energy intake, fiber, alcohol

**Confounders NOT accounted for:**

- Key confounders: N/A
- Other factors considered: timing, temporal use, sugar, protein, energy density, medications, supplements

**Additional model adjustments:**

Percentage of fat from energy, presence of disease (diabetes and hypertension)

**Limitations:**

- Attrition 18% without information on non-completers
- Start of follow-up differed among participants
- Not generalizable to other racial/ethnic groups
- No preregistered data analysis plan

**Funding sources:**

Basic Science Research Program of the National Research Foundation of Korea funded by the Ministry of Education, Science and Technology



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Kärkkäinen, 2018<sup>114</sup></b>  <b>Prospective Cohort Study, FinnTwin16, Finland</b>  Baseline N=4679, Analytic N=3490 (Attrition: 25%); Power: NR</p> <p><b>Recruitment:</b> Central Population Registry of Finland</p> <p><b>Participant characteristics: young adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 52%</li> <li>• Age: ~24y</li> <li>• Race/ethnicity: NR</li> <li>• SES: 57% High school education</li> <li>• Anthropometrics: 18% Overweight, 4% Obesity</li> <li>• Physical activity: ~5.0 MET</li> <li>• Smoking: ~28%</li> </ul> <p><b>Summary of findings:</b>  In young adults, greater sweet drink intake was associated with lower odds of weight maintenance (vs weight gain) among women at 10y follow-up. (In essence, women who consumed more SSBs at age ~24y had greater odds of weight gain over the following 10 years than those who consumed less.) There was no association between sweet drink intake and weight maintenance among men.</p>	<p><b>Exposure of interest:</b> Sweet drinks (sugared soft drinks or juices)</p> <p><b>Comparator:</b> Sweet drink intake (continuous)</p> <p>Other exposure measures: N/A</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Modified FFQ; represents frequency of consumption</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Sweet drink: NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline (Wave 4, age ~24y), 10y follow-up (Wave 5, age ~34y)</li> <li>• Height and weight were self-reported</li> <li>• BMI calculated as kg/m<sup>2</sup></li> <li>• Waist circumference was self-reported: participants were sent a tape measure along with illustrated instructions</li> <li>• BMI &amp; waist circumference were validated in a measured sub-sample</li> <li>• Weight status based on standard WHO definitions: Underweight (BMI &lt; 19.5 kg/m<sup>2</sup>), Normal weight (BMI 19.5-24.9 kg/m<sup>2</sup>), Overweight (BMI 25-29.9 kg/m<sup>2</sup>), and Obesity (BMI &gt;29.9 kg/m<sup>2</sup>)</li> <li>• Weight maintenance defined as weight maintained within ±5% of baseline BMI</li> </ul>	<p><b>Weight maintenance vs weight gain over 10 years</b>, Logistic regression, OR (95% CI)</p> <p><b>Women: 0.79 (0.67, 0.93)</b></p> <p>Men: 1.14 (0.97, 1.34)</p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, race/ethnicity</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Health foods, high fat foods, sweet foods, meat, daily breakfast, regularity of eating, control in eating, history of dieting, disinhibited eating, children, life satisfaction, self-rated health</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Missing data: participants who were excluded were more educated and less likely to smoke</li> <li>• Validity of FFQ unclear</li> <li>• Exposure data only measured at baseline</li> <li>• Exposure status not well described</li> <li>• Weight, height, and waist circumference were self-reported</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NR</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Ma, 2016<sup>118</sup></b>  <b>Prospective Cohort Study, Third Generation cohort of the Framingham Heart Study, United States</b>  Analytic N=1003 (Attrition: NR); Power: NR</p> <p><b>Recruitment:</b> mail to children of the Offspring Cohort</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: ~1900 kcal/d</li> <li>Sex (female): 45%</li> <li>Age: Mean=45.3y</li> <li>Race/ethnicity: 99.7% White</li> <li>SES: NR</li> <li>Anthropometrics: BMI ~27.4 kg/m<sup>2</sup></li> <li>Physical activity: Score ~37.2</li> <li>Smoking: 9% Current smoker</li> </ul> <p><b>Summary of findings:</b>  In adults, SSB intake was not significantly associated with changes in body weight at 6y follow-up.</p>	<p><b>Exposure of interest:</b> SSB intake (caffeinated colas with sugar, caffeine-free colas with sugar, other carbonated beverages with sugar, fruit punches, lemonade, or other noncarbonated fruit drinks; did not include sports drinks, energy drinks, and sweetened teas)</p> <p><b>Comparator:</b> SSB intake (categorical):</p> <ul style="list-style-type: none"> <li>Non-consumers (none to &lt;1 svg/mo): Median 0 svg/wk</li> <li>Occasional consumers (1 svg/mo to &lt;1 svg/wk): Median 0.5 svg/wk</li> <li>Frequent consumers (1 svg/wk to 1 svg/d): Median 3 svg/wk</li> <li>Daily consumers (≥1 svg/d): 11 svg/wk</li> </ul> <p>Other exposure measures: diet soda</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Harvard semi-quantitative FFQ (validated)</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>SSB intake: 32% Non-consumers, 20% Occasional consumers, 35% Frequent consumers, 13% Daily consumers</li> </ul> <p>Note: intake also stratified by sex in paper</p> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (2002-2005), ~6y follow-up (2008-2011)</li> <li>Height measured to nearest ¼ inch using vertical ruler</li> <li>Weight measured with light clothes and rounded to nearest 0.5 pound</li> <li>BMI calculated as kg/m<sup>2</sup></li> </ul>	<p><b>Weight</b>, kg, Linear regression, <math>\beta</math> (95% CI)  <b>Change per frequency of SSB intake:</b>  Non-consumers: 2.4 (1.7, 3.2)  Occasional consumers: 2.8 (1.8, 3.7)  Frequent consumers: 2.4 (1.7, 3.0)  Daily consumers: 1.7 (0.5, 2.9)  P trend = 0.26  P interaction (Sex) = 0.46  P interaction (BMI) = 0.88  P interaction (T2DM) = 0.34</p> <p><b>MEN</b>  Non-consumers: 3.1 (2.0, 4.3)  Occasional consumers: 2.4 (1.1, 3.7)  Frequent consumers: 2.7 (1.9, 3.4)  Daily consumers: 2.5 (1.2, 3.8)  P trend = 0.77</p> <p><b>WOMEN</b>  Non-consumers: 1.8 (0.8, 2.7)  Occasional consumers: 2.5 (1.2, 3.7)  Frequent consumers: 2.1 (0.8, 3.4)  Daily consumers: 1.2 (-1.6, 4.0)  P trend = 0.72</p> <p><u>Data on change in visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) are also included in the paper</u></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, (race/ethnicity), anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, supplements, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications</li> </ul> <p><b>Additional model adjustments:</b>  Saturated fat intake, diet soda intake, whole grain, fruit, vegetable, coffee, nuts, and fish</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Follow-up time differs among participants</li> <li>Exposure measured at baseline only</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NHLBI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Olsen, 2016</b><sup>125</sup></p> <p><b>Prospective Cohort Study, Danish part of Monitoring Trends and Determinants of Cardiovascular Disease (MONICA) + Diet, Cancer, and Health (DCH) study + Inter99 clinical trial study, Denmark</b></p> <p>MONICA: Analytic N=1257 (Overall trial attrition: ~17% ); Power: NR DCH: Baseline N=NR, Analytic N=2167 (Attrition: NR%); Power: NR Inter99: Analytic N=1341 (Attrition: NR ); Power: NR</p> <p><b>Recruitment:</b> random sampling in the former Copenhagen or Aarhus Counties</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~9.0 MJ/d</li> <li>• Sex (female): ~51%</li> <li>• Age: ~48y</li> <li>• Race/ethnicity: NR</li> <li>• SES: ~31% Primary school or less</li> <li>• Anthropometrics: Weight ~78 kg</li> <li>• Physical activity: 15% Most sedentary group</li> <li>• Smoking: ~35% Never smokers</li> </ul> <p><b>Summary of findings:</b></p> <p>In adults, increased soft drink intake was significantly associated with greater weight gain over time in a sample with self-reported weight. (This sample was also older, less sedentary, and more likely to have never smoked than the other two cohorts considered.) There was no significant association between weight change and soft drink intake for the other two cohorts, nor was there a significant association between soft drink intake and waist circumference in any cohort.</p>	<p><b>Exposure of interest:</b> Soft drink intake with caloric sweeteners (1 svg= 200 g/d)</p> <p><b>Comparator:</b> continuous (svg/d)</p> <p>Other exposure measures: N/A</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Validated FFQ (in DCH and Inter99) and 7d food record (in MONICA) with unclear validation; represents usual intake in previous year or month</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b> g/d, Median (5<sup>th</sup>%, 95<sup>th</sup>%)</p> <ul style="list-style-type: none"> <li>• Soft drink intake: <ul style="list-style-type: none"> <li>○ MONICA: 0 (0, 250)</li> <li>○ DCH: 10.5 (0.3, 200.3)</li> <li>○ Inter99: 16.4 (0, 500)</li> </ul> </li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, and follow-up (varied)</li> <li>• Weight and height were self-reported reported in DCH, and measured according to baseline procedures (in MONICA and Inter99)</li> <li>• Waist circumference (WC) was self-reported reported in DCH after receipt of instructions at umbilicus level; for Inter99, WC was measured horizontally midway between lower rib margin and iliac crest to nearest 1 cm; WC was not measured in MONICA</li> </ul>	<p><b>Weight change</b>, kg/y, Annual change per svg/d increase, Linear regression, <math>\beta</math> (95% CI)</p> <p><b>TEI Unadjusted</b> MONICA: 0.04 (-0.06, 0.14), P=0.45 <b>DCH: 0.10 (0.01, 0.18), P=0.02</b> Inter99: -0.03 (-0.19, 0.13), P=0.70</p> <p><b>TEI Adjusted</b> MONICA: 0.05 (-0.05, 0.14), P=0.38 <b>DCH: 0.12 (0.03, 0.20), P=0.01</b> Inter99: -0.02 (-0.19, 0.15), P=0.82</p> <p><b>WC change (adjusted for BMI)</b>, cm/y, Annual change per svg/d increase, Linear regression, <math>\beta</math> (95% CI)</p> <p><b>TEI Unadjusted</b> DCH: -0.02 (-0.13, 0.08), P=0.69 Inter99: 0.05 (-0.09, 0.20), P=0.46</p> <p><b>TEI Adjusted</b> DCH: -0.02 (-0.13, 0.08), P=0.67 Inter99: 0.09 (-0.06, 0.24), P=0.26</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b> Menopausal status (in women)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No information on non-completers</li> <li>• Methods of exposure assessment were not similar; unclear validation of method in MONICA</li> <li>• Exposure measured only at baseline</li> <li>• Methods of outcome assessment were not similar; weight and height was self-reported in DCH</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b> Danish Council for Strategic Research; Danish Cancer Society; Danish Medical Research Council; Danish Centre for Evaluation and Health Technology Assessment; Novo Nordisk; Copenhagen County; Danish Heart Foundation; Danish Pharmaceutical Association; Augustinus Foundation; Henriksen Foundation; Becket Foundation</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Pan, 2013<sup>46</sup></b>  <b>Prospective Cohort Study, Nurses Health Study (NHS) + NHS II + Health Professionals Follow-Up Study (HPS), United States</b>  <i>NHS</i>: Baseline N=121,700 Analytic N=50,013 (Attrition: 58.9%); Power: NR  <i>NHS II</i>: Baseline N=116,671 Analytic N=52,987 (Attrition: 54.6%); Power: NR  <i>HPS</i>: Baseline N=51,529 Analytic N=21,988 (Attrition: 57.3%); Power: NR</p> <p><b>Recruitment:</b> professional organizations or from occupation mailing house lists</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 82%</li> <li>• Age: Mean~47y</li> <li>• Race/ethnicity: primarily white</li> <li>• SES: primarily educated</li> <li>• Anthropometrics: Overweight 31%, Obesity 17%, BMI: Mean~25 kg/m<sup>2</sup></li> <li>• Physical activity: Mean~18 MET-hr/wk</li> <li>• Smoking: Never smoker 54%, Past smoker 33%, Current smoker 13%</li> </ul> <p><b>Summary of findings:</b>  In adults, when stratified by age or baseline BMI, SSB intake was significantly associated with weight gain.</p>	<p><b>Exposure of interest:</b> SSB intake (“Coke, Pepsi or other cola with sugar”, “caffeine-free Coke, Pepsi or other cola with sugar”, “other carbonated beverages with sugar”, and “Hawaiian punch, lemonade or other non-carbonated fruit drinks”)</p> <p><b>Comparator:</b> SSB intake (continuous; svg/d)</p> <p>Other exposure measures: milk, water, diet beverages, fruit juice, coffee, tea</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated FFQ; represents usual intake of foods and beverages</li> <li>• At baseline, every 4y over 16- to 20-y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• SSB intake, svg/d, Mean (5<sup>th</sup>-95<sup>th</sup>%):  <i>NHS</i> 0.24 (0-1.07), <i>NHS II</i> 0.46 (0-2.5), <i>HPS</i> 0.37 (0-1.36)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, and every 2y over 16- to 20-y follow-up</li> <li>• Weight was collected via self-report from questionnaire</li> </ul>	<p><b>Weight</b>, kg, Linear regression, <math>\beta</math> (95% CI)  <b>Change per svg/d increase:</b>  <i>NHS</i>: 0.36 (0.30, 0.41), <i>P</i>=NR  <i>NHS II</i>: 0.47 (0.42, 0.52), <i>P</i>=NR  <i>HPS</i>: 0.25 (0.19, 0.31), <i>P</i>=NR  <b>Stratified by age:</b> <math>\leq 50y</math>, <math>&gt;50y</math>  <i>NHS</i>: 0.45 (0.35, 0.56), 0.35 (0.29, 0.42), <i>P</i>=0.13  <b><i>NHS II</i>: 0.47 (0.42, 0.52), 0.42 (0.28, 0.56), <i>P</i>=0.006</b>  <b><i>HPS</i>: 0.34 (0.23, 0.44), 0.21 (0.13, 0.29), <i>P</i>=0.004</b></p> <p><b>Stratified by BMI (kg/m<sup>2</sup>):</b> <math>&lt;25</math>, 25-29.9, <math>\geq 30</math>  <b><i>NHS</i>: 0.13 (0.07, 0.18), 0.40 (0.31, 0.49), 0.56 (0.39, 0.72), <i>P</i>&lt;0.001</b>  <b><i>NHS II</i>: 0.15 (0.11, 0.20), 0.53 (0.44, 0.62), 0.81 (0.68, 0.94), <i>P</i>&lt;0.001</b>  <b><i>HPS</i>: 0.12 (0.05, 0.19), 0.27 (0.18, 0.36), 0.45 (0.16, 0.74), <i>P</i>&lt;0.001</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: sugar, protein, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES</li> <li>• Other factors considered: total energy intake, timing, temporal use, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Television watching, dietary variables (fruits, vegetables, whole grain, refined grain, potatoes, potato chips, red meat, other dairy products, sweets and deserts, nuts, fried foods, and trans fat), other beverage variables</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Weight was self-reported</li> </ul> <p><b>Funding sources:</b>  NIH</p>

Qi, 2012<sup>127</sup>

**Prospective Cohort Study, Nurses Health Study (NHS) + Health Professionals Follow-Up Study (HPFS) + Women's Genome Health Study (WGHS), United States**

NHS: Analytic N=6934 (Attrition: NR);  
Power: NR  
HPFS: Analytic N=4423 (Attrition: NR);  
Power: NR  
WGHS: Analytic N=21740 (Attrition: NR);  
Power: NR

**Recruitment:** professional organizations or from occupation mailing house lists

**Participant characteristics: adults**

- Total energy intake: ~1700 kcal/d
- Sex (female): 87%
- Age: Mean~51y
- Race/ethnicity: 100% European ancestry
- SES: all health professionals
- Anthropometrics: BMI: Mean~25 kg/m<sup>2</sup>
- Physical activity: Mean~16 MET-hr/wk
- Smoking: Current smoker ~9%

**Summary of findings:**

Greater SSB intake was significantly associated with increased BMI and higher incident obesity over time in adults. This relationship was significantly stronger for individuals with greater genetic predisposition of obesity.

[Note: Analyses first run in NHS & HPFS, then repeated in WGHS to replicate results. Exposure data used to predict prospective change in BMI in 4y chunks in NHS & HPFS. Genetic predisposition scores calculated based on obesity-

**Exposure of interest:** SSB intake (caffeinated colas, caffeine-free colas, carbonated non-cola soft drinks, and non-carbonated SSBs (fruit punches, lemonades, and other fruit drinks))

**Comparators:**

- SSB intake (continuous; svg/d)
- SSB intake (categorical; servings):
  - <1 svg/mo
  - 1-4 svg/mo
  - 2-6 svg/wk
  - ≥1 svg/d

Other exposure measures: artificially-sweetened beverages

**Exposure assessment method and timing:**

- Validated semi quantitative FFQ
- At baseline, and every 4y after for NHS and HPFS
- At baseline only for WGHS

**Study beverage intake:** svg/d, Mean (SD)

- SSB intake at baseline:
  - NHS: <1 svg/mo (41%), 1-4 svg/mo (26%), 2-6 svg/wk (22%), ≥1 svg/d (12%)
  - HPFS: <1 svg/mo (37%), 1-4 svg/mo (24%), 2-6 svg/wk (30%), ≥1 svg/d (9%)
  - WGHS: <1 svg/mo (45%), 1-4 svg/mo (22%), 2-6 svg/wk (25%), ≥1 svg/d (8%)

**Outcome assessment methods/timing:**

- NHS: At baseline, and every 4y follow-up assessment up to 18y
- HPFS: At baseline, and every 4y follow-up assessment up to 12y
- WGHS: At baseline, and 6y follow-up
- Height and weight were self-reported and highly correlated (0.97) with measured values in a sub-sample
- BMI calculated as kg/m<sup>2</sup>

Data represent the difference in BMI for each increment of 10 risk alleles, stratified by beverage intake. **P for interaction (genetic predisposition score\*beverage intake)**

**Increase in BMI**, Linear regression, β (SE)

NHS (n=6934)

<1 svg/mo: 1.18 (0.17)  
1-4 svg/mo: 1.56 (0.16)  
2-6 svg/wk: 1.78 (0.22)  
≥1 svg/d: 2.03 (0.38)  
**P for interaction = 0.008**

HPFS (n=4432)

<1 svg/mo: 0.77 (0.19)  
1-4 svg/mo: 0.43 (0.20)  
2-6 svg/wk: 1.08 (0.19)  
≥1 svg/d: 1.54 (0.37)  
**P for interaction = 0.02**

WGHS (n=21,740)

<1 svg/mo: 1.39 (0.13)  
1-4 svg/mo: 1.64 (0.19)  
2-6 svg/wk: 1.90 (0.18)  
≥1 svg/d: 2.53 (0.36)  
**P for interaction = 0.001**

**Incident Obesity**, Cox proportional hazard, RR (95% CI)

NHS (n=6402): Data NR, P for interaction=0.03

HPFS (n=3889): Data NR, P interaction=0.20

WGHS (n=18,127):

<1 svg/mo: 1.40 (1.19, 1.64)  
1-4 svg/mo: 1.50 (1.16, 1.93)  
2-6 svg/wk: 1.54 (1.21, 1.94)  
≥1 svg/d: 3.16 (2.03, 4.92)  
**P for interaction =0.007**

**TEI adjusted:** Yes

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity, smoking
- Other factors considered: total energy intake, alcohol

**Confounders NOT accounted for:**

- Key confounders: SES
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements

**Additional model adjustments:**

Source of genotyping data or eigenvectors derived from GWAS, time spent watching television (for NHS and HPFS), Alternative Healthy Eating Index score (for NHS and HPFS), and geographic region (for WGHS)

**Limitations:**

- Not all key confounders accounted for
- Weight and height self-reported
- No preregistered data analysis plan

**Funding sources:**

NIH; Merck Research Laboratories; American Heart Association; Harvard Glaucoma Center of Excellence; Amgen

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
related SNPs; each point of the genetic-predisposition score corresponded to one risk allele.]	<ul style="list-style-type: none"> <li>Obesity (BMI&gt;30 kg/m<sup>2</sup>)</li> </ul>	<p><b>Difference in BMI, per 1 svg/d of SSB according to genetic predisposition score quartile, kg/m<sup>2</sup>, General linear model</b></p> <p><b>NHS: Data NR, P for interaction&lt;0.001</b></p> <p>HPFS: Data NR, P for interaction=0.09</p> <p><b>WGHS: Data NR; P for interaction=0.003</b></p>	



**Stern, 2017<sup>131</sup>**

**Prospective Cohort Study, Mexican Teachers' Cohort, Mexico**

Baseline N=27992, Analytic N=11218 for weight and N=9294 for WC (Attrition: 60% weight, 67% WC); Power: NR

**Recruitment:** female teachers from Jalisco and Veracruz, Mexico

**Participant characteristics: Hispanic females living in Mexico**

- Total energy intake: 1756 (614) kcal/d
- Sex (female): 100%
- Age: 43.3 (5.2) y; Range 25-64
- Race/ethnicity: 100% Hispanic
- SES: NR
- Anthropometrics: BMI 27.2 (4.4) kg/m<sup>2</sup>; 42% Overweight, 23% Obese
- Physical activity: High 34%, Medium 37%, Low 29%
- Smoking: Never 81%, Current 8%

**Summary of findings:**

In Hispanic females living in Mexico, an increase of 1 svg/d of sugar-sweetened soda consumption was significantly associated with an increase in weight and waist circumference over a 2-yr period. Compared to no change in intake, a decrease in sugar-sweetened soda consumption by more than 1 svg/wk was significantly associated with less weight gain and decreased change in waist circumference over a 2-yr period.

**Exposure of interest:** Sugar-sweetened soda

**Comparators:**

- Sugar-sweetened soda intake (continuous; svg/d):
- Sugar-sweetened soda intake (categorical; svg/wk):
  - Decreased (<-1 svg/wk)
  - No change (-1 to +1 svg/wk)
  - Increased (>1 svg/wk)

Other exposure measures: sugar-free soda

**Exposure assessment method and timing:**

- Semi-quantitative FFQ; represents intake over previous year; validated
- In 2006 and 2008

**Study beverage intake:** Mean (SD)

- Sugar-sweetened soda: 0.4 (0.5) svg/d

**Outcome assessment methods/timing:**

- In 2006 and 2008
- Height (in cm) and weight (in kg) were self-reported
- Waist circumference (WC, in cm) was self-reported; participants were provided a plastic measuring tape and instructions to assess their WC

**Weight, kg, Change from 2006–2008,**

Linear regression,  $\beta$  (95% CI)

**Per 1 svg/d increase: 1.0 (0.7, 1.2), P<0.001**

**Per change in svg/wk:**

- No change (-1 to +1, n=6409): Ref
- **Decreased (<1, n=3075): -0.4 (-0.6, -0.2)**
- **Increased (>1, n=1734): 0.3 (0.2, 0.5)**

**Per 1 svg/d increase, stratified by age:**

Baseline age  $\geq$ 43y: 1.2 (0.8, 1.5)

Baseline age <43y: 0.8 (0.4, 1.1)

P for heterogeneity: 0.05

**Per 1 svg/d increase, stratified by BMI:**

Obese ( $\geq$ 30 kg/m<sup>2</sup>): 1.5 (1.0, 2.0)

Overweight (25-29.9 kg/m<sup>2</sup>): 1.0 (0.6, 1.3)

Normal (<25 kg/m<sup>2</sup>): 0.6 (0.3, 1.0)

P for heterogeneity: 0.003

**WC, cm, change from 2006–2008,**

linear regression,  $\beta$  (95% CI)

**Per 1 svg/d increase: 0.9 (0.5, 1.4), P<0.001**

**Per change in svg/wk:**

- No change (-1 to +1, n=5350): Ref
- **Decreased (<1, n=2538): -0.5 (-0.9, -0.1)**
- **Increased (>1, n=1406): 0.3 (0.1, 0.6)**

**Per 1 svg/d increase, stratified by age:**

Baseline age  $\geq$ 43y: 1.0 (0.4, 1.7)

Baseline age <43y: 0.9 (0.2, 1.5)

P for heterogeneity: 0.67

**Per 1 svg/d increase, stratified by BMI:**

**TEI adjusted:** No

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity, smoking
- Other factors considered: alcohol

**Confounders NOT accounted for:**

- Key confounders: SES
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements

**Additional model adjustments:**

Sugar-free soda consumption, state of residency, oral contraceptive use, menopausal status, postmenopausal hormone therapy use, food and beverage intake (red meat, dairy, yogurt, fruit, vegetables, nuts, white bread, flour tortillas, corn tortillas, orange or grapefruit juice, and homemade sweetened beverages)

**Limitations:**

- One key confounder not accounted for
- Attrition 60% without information on non-completers
- Weight, height, and waist circumference self-reported
- No preregistered data analysis plan

**Funding sources:**

AstraZeneca; Bloomberg Philanthropies (National Institute of Public Health in Mexico); Bernard Lown Scholars Program in Cardiovascular Health; American Institute of Cancer Research; Consejo Nacional de Ciencia y Tecnología; NIH

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
		<p>Obese (<math>\geq 30</math> kg/m<sup>2</sup>): 1.2 (0.3, 2.2)  Overweight (25-29.9 kg/m<sup>2</sup>): 1.1 (0.4, 1.8)  Normal (&lt;25 kg/m<sup>2</sup>): 0.6 (-0.2, 1.4)  P for heterogeneity: 0.54</p> <p>“Exclusion of women who developed chronic conditions in the 2-year period did not result in relevant changes in our estimates.”</p>	



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Tucker, 2015</b><sup>136</sup></p> <p><b>Prospective Cohort Study, United States</b></p> <p>Baseline N=228, Analytic N=170 (Attrition: 25%); Power: 170 participants produced statistical power of .92 to detect an effect size of .3 with participants divided into four groups and <math>\alpha = 0.05</math>.</p> <p><b>Recruitment:</b> ~20 cities in Utah and Wyoming using newspaper ads, e-mails, flyers, and word of mouth</p> <p><b>Participant characteristics: healthy women</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: 2017 (324) kcal/d</li> <li>• Sex (female): 100%</li> <li>• Age: 41.5 (3.0) y; Range 35-45y</li> <li>• Race/ethnicity: ~90% non-Hispanic white</li> <li>• SES: 31% Some college education, 82% Married</li> <li>• Anthropometrics: NR</li> <li>• Physical activity: 2581611 (823095) activity counts on accelerometer</li> <li>• Smoking: 100% nonsmokers (inclusion criteria)</li> </ul> <p><b>Summary of findings:</b></p> <p>In women, sugar-sweetened soft drink intake was significantly associated with increased body weight compared to artificially sweetened soft drink intake or no soft drink intake at 4y follow-up.</p>	<p><b>Exposure of interest:</b> Sugar-sweetened soft drink intake (12-oz serving)</p> <p><b>Comparators:</b> Type of soft drink typically consumed (categorical):</p> <ul style="list-style-type: none"> <li>• None</li> <li>• Artificially sweetened</li> <li>• Mixed (sugar and artificially sweetened)</li> </ul> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Six questions on frequency, type, and size of soft drink intake; represents weekly consumption</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Soft drink intake (12-oz serving): <ul style="list-style-type: none"> <li>◦ &lt;0.5/wk: 36%</li> </ul> Of regular consumers: <ul style="list-style-type: none"> <li>◦ 0.5-1/wk: 55.7%</li> <li>◦ 2-6/wk: 25.3%</li> <li>◦ ≥7/wk: 19%</li> </ul> </li> <li>• 40.5% primarily consumed sugar-sweetened soft drinks</li> <li>• 41.8% primarily consumed artificially sweetened soft drinks</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 4y follow-up</li> </ul> <p>Weight measured to the nearest 0.05 kg using computerized electronic scale; all participants used restroom before being weight, wore lightweight nylon swimsuit issue by lab, and were instructed not to eat 3hr prior</p>	<p><b>Weight</b>, kg, Change per type of soft drink consumed, Multiple regression, <math>\beta</math> (SE)</p> <p><b>TEI unadj:</b></p> <p><i>Sugar-sweetened vs No soft drinks:</i>  <b>2.68 (5.14) vs 0.50 (5.05), <math>P &lt; 0.05</math></b></p> <p><i>Sugar-sweetened vs Artificially-sweetened:</i> <b>2.68 (5.14) vs -0.05 (4.40), <math>P &lt; 0.05</math></b></p> <p><i>Sugar-sweetened vs Mixed soft drinks:</i>  2.68 (5.14) vs 1.22 (5.06), NS</p> <p><b>TEI adjusted:</b> “relationship between soft drink consumption and changes in body weight was weakened by 28% and was no longer statistically significant”  <math>P = 0.051</math></p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Menopause status</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Attrition 25% without information on non-completers</li> <li>• Exposure data collection tool not validated</li> <li>• Exposure only measured at baseline</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NR</p>

**Table 19. Risk of bias for randomized controlled trials examining SSB consumption versus different amount or water consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>xlii, xliii</sup>**

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Maersk, 2012 <sup>120</sup>	High	Some Concerns	Some Concerns	Low	Some Concerns
Tate, 2012 <sup>133</sup>	Low	Low	Low	Low	Some Concerns
Vazquez-Duran, 2016 <sup>137</sup>	Low	Low	Low	Low	Low

<sup>xlii</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xliii</sup> Possible ratings of low, some concerns, or high determined using the "[Cochrane Risk-of-bias 2.0](#)" (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). *Cochrane Methods. Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). [dx.doi.org/10.1002/14651858.CD201601](https://doi.org/10.1002/14651858.CD201601).)

**Table 20. Risk of bias for the non-randomized controlled trial examining SSB consumption versus different amount or water consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>xliv, xlv</sup>**

	Confounding	Selection of participants	Classification of interventions	Deviations from intended interventions	Missing data	Outcome measurement	Selection of the reported result
Partridge, 2016 <sup>126</sup>	Serious	Low	Low	Low	Moderate	Serious	Moderate

<sup>xliv</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xliv</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the “[Risk of Bias in Non-randomized Studies of Interventions \(ROBINS-I\) tool](#)” (Sterne JAC, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JPT. ROBINS-I: a tool for assessing risk of bias in non-randomized studies of interventions. *BMJ* 2016; 355; i4919; doi: 10.1136/bmj.i4919.)

**Table 21. Risk of bias for prospective cohort studies examining SSB consumption versus different amount or water consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>xlvi, xlvii</sup>**

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Appelhans, 2017 <sup>86</sup>	Serious	Moderate	Low	Low	Moderate	Low	Moderate
Auerbach, 2018 <sup>64</sup>	Moderate	Low	Low	Low	Low	Low	Moderate
Barone Gibbs, 2012 <sup>87</sup>	Serious	Low	Low	Low	Low	No Information	Moderate
Barrio-Lopez, 2013 <sup>88</sup>	Serious	Low	Low	Low	Low	Serious	Moderate
Boggs, 2013 <sup>90</sup>	Moderate	Moderate	Low	Low	Low	Serious	Moderate
Bundrick, 2014 <sup>91</sup>	Serious	Low	Low	Moderate	Moderate	Low	Serious
Carroll, 2018 <sup>94</sup>	Serious	Low	Serious	Moderate	Low	Low	Moderate
Cleland, 2018 <sup>96</sup>	Serious	Low	Critical	Low	Moderate	Serious	Moderate
Ferreira-Pego, 2016 <sup>68</sup>	Serious	Moderate	Low	Moderate	Low	Low	Moderate
Fowler, 2015 <sup>104</sup>	Moderate	Low	Moderate	Low	Low	Low	Moderate
French, 2012 <sup>105</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Fresan, 2016 <sup>22</sup>	Serious	Moderate	Low	Low	Low	Moderate	Moderate
Funtikova, 2015 <sup>23</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Gearon, 2018 <sup>106</sup>	Serious	Moderate	Moderate	Moderate	Moderate	Low	Moderate
Kaikkonen, 2015 <sup>31</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Kang, 2017 <sup>113</sup>	Moderate	Moderate	Low	Low	Moderate	Low	Moderate
Kärkkäinen, 2018 <sup>114</sup>	Serious	Low	Serious	Moderate	Moderate	Serious	Moderate
Ma, 2016 <sup>118</sup>	Serious	Moderate	Low	Moderate	Low	Low	Moderate
Olsen, 2016 <sup>125</sup>	Serious	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

<sup>xlvi</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>xlvi</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

Pan, 2013 <sup>46</sup>	Serious	Moderate	Low	Low	Low	Serious	Moderate
Qi, 2012 <sup>127</sup>	Moderate	Low	Low	Low	Moderate	Moderate	Moderate
Stern, 2017 <sup>131</sup>	Serious	Low	Low	Low	Moderate	Serious	Moderate
Tucker, 2015 <sup>136</sup>	Serious	Low	Moderate	Moderate	Moderate	Low	Moderate

**Table 22: Summary of articles examining the relationship between SSB consumption versus LNCSB and growth, size, body composition and risk of overweight and obesity in children<sup>xlvi</sup>**

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
CONTROLLED TRIALS			

<sup>xlvi</sup> Abbreviations: BMIZ: BMI z-score; d: day(s); mo: month(s); NA: not applicable; RCT: randomized controlled trial; SD: standard deviation; SES: socioeconomic status; SSB: sugar-sweetened beverage; WC: waist circumference; y: year(s)  
 Red font indicates a statistically significant detrimental relationship, and green font indicates a statistically significant beneficial relationship.

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**De Ruyter, 2012<sup>98\*</sup>** (see **Katan, 2016<sup>115</sup>**)

**RCT, Double-blind Randomized Intervention study in Kids (DRINK) secondary analysis, the Netherlands**  
Baseline N=641, Analytic N=477; Attrition: 26%; Power: sample size calculation is 212 subjects per treatment, power=0.8;  $\alpha=0.05$

**Recruitment:** 8 elementary schools in an urban area near Amsterdam

**Participant characteristics: children who commonly drank SSBs**

- Total energy intake: NR
- Sex (female): 47%
- Age: 8.2 (1.8) y
- Race/ethnicity: ~78% Dutch ancestry; ~22% Non-Western ancestry
- SES: Parent education: ~55% college or university degree; ~33% high school diploma; ~14% elementary, vocational
- Anthropometrics: BMI ~16.9 kg/m<sup>2</sup>
- Physical activity: NR
- Smoking: NR

**Summary of findings:**

In children, consuming 8oz/d of a SSB compared to a sugar-free beverage over 18 months resulted in increased BMIZ, sum of skinfolds, waist-to-height ratio, fat mass (both kg and %), waist circumference, and weight. It also resulted in a smaller increase in height.

\* Some info on baseline data and methodology from: Effect of sugar-sweetened beverages on body weight in children: design and baseline characteristics of the Double-blind, Randomized Intervention study in Kids. *Contemp Clin Trials* 2012;33:247-57.

**Intervention (Sugar-free group):**

Artificially-sweetened, non-carbonated beverage; 1 can/d provided (8oz, 250 mL/d), n=319

**Comparator (Sugar group):** Sugar-containing, non-carbonated beverage; 1 can/d provided (8oz, 250 mL/d), n=322

Intervention duration: 18mo

Intervention compliance: calculated adherence rate per child during school days from the number of cans returned empty, half-filled, or full during one randomly selected week each month; 26% of participants stopped consuming the study beverage

**Study beverage intake:**

- SSBs in classroom at 10am break: 1.02 (0.20); SSB/wknd day: 1.50 (1.40)

**Outcome assessment methods/timing:**

- At baseline, 6, 12, 18 mo
- Weight, height, skinfold thickness (of the biceps, triceps, and subscapular and suprailiac regions), waist circumference, and arm-to-leg electrical impedance by trained researchers
- BMI z score: number of SD by which the BMI differed from the mean for a child's age and sex in the Netherlands
- Fat mass: determined by electrical impedance

**BMIZ, Mean (SD)**

**Within group:** 0mo, 18mo  
Sugar: 0.01 (1.04), 0.15 (1.06)  
Sugar-free: 0.06 (1.00), 0.08 (0.99)  
**Between groups,  $\Delta$ from baseline:**  
**P=0.001**

**Sum skinfolds, mm, Mean (SD)**

**Within group:** 0mo, 18mo  
Sugar: 35.6 (17.9), 41.1 (21.1)  
Sugar-free: 36.4 (17.7), 39.6 (20.4)  
**Between groups,  $\Delta$ from baseline:**  
**P=0.02**

**Waist-to-height ratio, %, Mean (SD)**

**Within group:** 0mo, 18mo  
Sugar: 44.2 (4.0), 43.7 (4.0)  
Sugar-free: 44.6 (4.0), 43.7 (4.0)  
**Between groups,  $\Delta$ from baseline:**  
**P=0.05**

**Fat mass, kg, Mean (SD)**

**Within group:** 0mo, 18mo  
Sugar: 5.70 (3.68), 7.28 (4.89)  
Sugar-free: 5.76 (3.85), 6.77 (4.71)  
**Between groups,  $\Delta$ from baseline:**  
**P=0.02**

**Fat mass, %, Mean (SD)**

**Within group:** 0mo, 18mo  
Sugar: 17.67 (6.92), 18.05 (8.25)  
Sugar-free: 17.91 (7.01), 17.22 (8.44)  
**Between groups,  $\Delta$ from baseline:**  
**P=0.02**

**WC, cm, Mean (SD)**

**Within group:** 0mo, 18mo  
Sugar: 58.69 (7.05), 62.72 (7.92)  
Sugar-free: 58.85 (7.44), 62.22 (7.97)  
**Between groups,  $\Delta$ from baseline:**  
**P=0.02**

**Weight, kg, Mean (SD)**

**Within group:** 0mo, 18mo  
Sugar: 30.33 (8.82), 37.69 (11.05)  
Sugar-free: 30.04 (8.93), 36.39 (10.41)  
**Between groups,  $\Delta$ from baseline:**  
**P<0.001**

**Height, cm, Mean (SD)**

**Within group:** 0mo, 18mo  
Sugar: 133.02 (12.71), 143.67 (13.05)  
Sugar-free: 132.06 (12.55), 142.34 (12.48)

**TEI adjusted:** No

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, anthropometry at baseline
- Other factors considered: medications

**Confounders NOT accounted for:**

- Key confounders: SES, physical activity, smoking
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, supplements, alcohol

**Additional model adjustments:** N/A

**Limitations:**

- Not all key confounders accounted for
- Drinks were designed for the study that may not be commercially available

**Funding Sources:**

Netherlands organization for Health Research and Development; Netherlands Heart Foundation; Royal Netherlands Academy of Arts and Sciences

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
		<p>Between groups, <math>\Delta</math>from baseline: P=0.04</p> <p><b>Height-Z</b>, Mean (SD)  <b>Within group:</b> 0mo, 18mo            Sugar: 0.03 (0.99), 0.09 (0.99)            Sugar-free: -0.09 (1.00), -0.07 (0.99)  <b>Between groups, <math>\Delta</math>from baseline:</b>            P=0.17</p>	



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Katan, 2016</b><sup>115*</sup> (see <b>De Ruyter, 2012</b><sup>98</sup>)  <b>RCT, Double-blind Randomized Intervention study in Kids (DRINK) secondary analysis, the Netherlands</b>  Baseline N=641, Analytic N=477; Attrition: 26%; Power: sample size calculation is 212 subjects per treatment, power=0.8; <math>\alpha=0.05</math>  <b>Recruitment:</b> 8 elementary schools in an urban area near Amsterdam</p> <p><b>Participant characteristics: children who commonly drank SSBs</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 47%</li> <li>• Age: 8.2 (1.8) y</li> <li>• Race/ethnicity: ~78% Dutch ancestry; ~22% Non-Western ancestry</li> <li>• SES: Parent education: ~55% college or university degree; ~33% high school diploma; ~14% elementary, vocational</li> <li>• Anthropometrics: BMI ~16.9 kg/m<sup>2</sup></li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  The impact of the consuming sugar-free beverages compared to SSBs was greater in children with initially higher BMI than children with lower BMI for BMIZ and waist circumference.  * Some info on baseline data and methodology from: Effect of sugar-sweetened beverages on body weight in children: design and baseline characteristics of the Double-blind, Randomized INtervention study in Kids. Contemp Clin Trials 2012;33:247-57.</p>	<p><b>Intervention (Sugar-free group):</b>  Artificially-sweetened, non-carbonated beverage; 1 can/d provided (8oz, 250 mL/d), n=319</p> <p><b>Comparator (Sugar group):</b> Sugar-containing, non-carbonated beverage; 1 can/d provided (8oz, 250 mL/d), n=322</p> <p><u>Intervention duration:</u> 18mo</p> <p><u>Intervention compliance:</u> calculated adherence rate per child during school days from the number of cans returned empty, half-filled, or full during one randomly selected week each month; 26% of participants stopped consuming the study beverage</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• SSBs in classroom at 10am break: 1.02 (0.20); SSB/wknd day: 1.50 (1.40)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 6, 12, 18 mo</li> <li>• Weight, height, skinfold thickness (of the biceps, triceps, and subscapular and suprailiac regions), waist circumference, and arm-to-leg electrical impedance by trained researchers</li> <li>• BMI z score: number of SD by which the BMI differed from the mean for a child's age and sex in the Netherlands</li> <li>• Fat mass: determined by electrical impedance</li> </ul>	<p>Lower BMI = below median; Higher BMI = above median  <u>Outcome:</u> difference in effect of treatment between children with lower vs higher BMI (95% CI)  <b>BMIZ: -0.16 (-0.31, -0.01), P=0.04</b>  <b>Weight (kg):</b> -0.90 (-1.95, 0.14), P=0.09  <b>Height (cm):</b> -0.02 (-0.70, 0.67), P=0.96  <b>Sum skinfolds (mm):</b> -2.94 (-6.16, -0.29), P=0.07  <b>WC (cm):</b> -1.19 (-2.21, -0.16), P=0.02  <b>Fat mass (kg):</b> -0.55 (-1.20, 0.10), P=0.10  <b>Fat mass (%):</b> -0.67 (-2.03, 0.69), P=0.33</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>• Other factors considered: medications</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Drinks were designed for the study that may not be commercially available</li> </ul> <p><b>Funding Sources:</b>  Netherlands organization for Health Research and Development; Netherlands Heart Foundation; Royal Netherlands Academy of Arts and Sciences</p>

**Table 23. Risk of bias for randomized controlled trials examining SSB consumption versus LNCSB and growth, size, body composition and risk of overweight and obesity in children<sup>xlix, l</sup>**

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
De Ruyter 2012 <sup>98</sup>	Low	Low	Low	Low	Low
Katan, 2016 <sup>115</sup>	Low	Low	Low	Low	Low

<sup>xlix</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>l</sup> Possible ratings of low, some concerns, or high determined using the "[Cochrane Risk-of-bias 2.0 \(RoB 2.0\)](#) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). *Cochrane Methods. Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). [dx.doi.org/10.1002/14651858.CD201601](https://doi.org/10.1002/14651858.CD201601).)

Table 24: Summary of articles examining the relationship between SSB consumption versus LNCSB and growth, size, body composition and risk of overweight and obesity in adults<sup>li</sup>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
CONTROLLED TRIALS			

<sup>li</sup> Abbreviations: ANOVA: analysis of variance; ASB: artificially-sweetened beverage; BMI: body mass index; CI: confidence interval; d: day(s); LCS: low calorie sweetener; NA: not applicable; NR: not reported; NS: not significant; RCT: randomized controlled trial; SD: standard deviation; SE: standard error; SEM: standard error of the mean; SES: socioeconomic status; SSB: sugar-sweetened beverage; SSSD: sugar sweetened carbonated soft drinks; TEI: total energy intake; USDA: U.S. Department of Agriculture; VAT: visceral adipose tissue; wk: week(s); y: year(s)  
Red font indicates a statistically significant detrimental relationship, and green font indicates a statistically significant beneficial relationship.

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Campos, 2015<sup>92</sup></b>  <b>RCT, Switzerland</b>  Baseline N=31, Analytic N= 27; Attrition: 13%; Power: NR</p> <p><b>Recruitment:</b> NR</p> <p><b>Participant characteristics: overweight and obese adults; consume <math>\geq 2</math> SSBs/d</b></p> <ul style="list-style-type: none"> <li>Total energy intake: ~2300 kcal/d</li> <li>Sex (female): 48%</li> <li>Age: NR</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI ~31 kg/m<sup>2</sup>; Weight ~92 kg</li> <li>Physical activity: ~9000 steps/d (sig diff between groups)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In overweight and obese adults that typically consumed two or more 22-oz SSBs per day, replacing SSBs with artificially sweetened beverages for 12 weeks did not result in a difference in body weight, BMI, fat mass%, fat-free mass%, or visceral adipose tissue compared to a control group that maintained usual SSB consumption.</p>	<p><b>Intervention (ASB):</b> replace habitual intake of SSBs with artificially sweetened beverages; Habitual intake = two or more 22-oz SSBs (carbonated soft drinks and sugar-sweetened tea); every week participants were given new batch of ASBs; n=14</p> <p><b>Comparator (control):</b> habitual intake of two or more 22-oz SSBs (carbonated soft drinks and sugar-sweetened tea); every week participants were given new batch of SSBs; n=13</p> <p><u>Intervention duration:</u> 12wk</p> <p><u>Intervention compliance:</u> &gt;90% based on returned packages</p> <p><b>Study beverage intake:</b> NR</p> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (wk4), 12wk follow-up (wk16)</li> <li>Weight and body composition (bioimpedancemetry) monitored every other week; Methods NR</li> <li>Body composition measured at wk4 (baseline), 10, and 16 (12wk follow-up); Methods NR</li> <li>Visceral adipose tissue (VAT) measured with MRS</li> </ul>	<p><b>Weight</b>, kg, Mean (SEM)  <b>Within group:</b> Wk4, Wk16  Control: 90.1 (4.0), 91.0 (3.9)  ASB: 95.1 (3.8), 93.7 (3.7)  <b>Change from baseline, between groups:</b> P=NS</p> <p><b>BMI</b>, kg/m<sup>2</sup>, Mean (SEM)  <b>Within group:</b> Wk4, Wk16  Control: 30.6 (1.5), 31.0 (1.4)  ASB: 31.5 (1.2), 31.0 (1.2)  <b>Change from baseline, between groups:</b> P=NS</p> <p><b>Fat mass %</b>, Mean (SEM)  <b>Within group:</b> Wk4, Wk16  Control: 34.1 (2.4), 34.8 (2.3)  ASB: 35.3 (1.8), 34.0 (2.1)  <b>Change from baseline, between groups:</b> P=NS</p> <p><b>Fat-free mass %</b>, Mean (SEM)  <b>Within group:</b> Wk4, Wk16  Control: 64.1 (2.7), 65.1 (2.3)  ASB: 64.6 (1.8), 65.9 (2.1)  <b>Change from baseline, between groups:</b> P=NS</p> <p><b>VAT</b>, cm<sup>3</sup>, Mean (SEM)  <b>Within group:</b> Wk4, Wk16  Control: 759.2 (165.5), 747.4 (156.7)  ASB: 684.2 (130.5), 582.4 (90.3)  <b>Change from baseline, between groups:</b> P=NS</p>	<p><b>TEI adjusted:</b> No  <b>Energy Intake, kcal/d, Mean (SD)</b>  <b>Within group:</b> 0wk, 10wk, 16wk  <b>SSB (control):</b> 2417.4 (137.5), 2225.4 (191.7), 2285.4 (190.1), P=NS  <b>ASB:</b> 2184.6 (157.7), 1709.2 (169.3), 1621.7 (164.7), P=NS  <b>Between groups:</b> P=NS</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, anthropometry at baseline</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: age, race/ethnicity, SES, physical activity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Randomization and allocation methods NR</li> <li>No power calculation</li> <li>Differential attrition: all non-completers from intervention group</li> <li>Outcome methods NR</li> <li>Trial registry did not include data analysis plan</li> </ul> <p><b>Funding Sources:</b>  Swiss National Foundation for Science; Fondation Raymond Berger pour la recherche sur le diabete et les maladies metaboliques</p>

**Higgins, 2019**<sup>108</sup>

**RCT, Beverage Consumption and Fine Motor Control clinical trial, United States**

Baseline N=154, Analytic N=123;  
Attrition: 20%; Power: >25 individuals per treatment group and ~4% variance (SD=1.78 kg body weight),  $\alpha$ <0.05, 80% power to detect differences in average weight gain of 2.8 kg

**Recruitment:** from Greater Lafayette, Indiana area

**Participant characteristics: adults with overweight or obesity**

- Total energy intake: ~2300 kcal/d
- Sex (female): 56%
- Age: ~28y
- Race/ethnicity: NR
- SES: NR
- Anthropometrics: BMI ~29 kg/m<sup>2</sup>
- Physical activity: Sport index ~2.5
- Smoking: NR

**Summary of findings:**

In adults with overweight or obesity, drinking sucrose-sweetened beverages (1 1.25-1.75/d) compared to low-calorie sweetened beverages (1.25-1.75 L/d) for 12wk resulted in greater increases in weight, BMI, total fat mass, and total fat-free mass. Energy intake was greater during the intervention in the group that drank sucrose-sweetened beverages compared to low-calorie sweetened beverages; this added EI was attributable to the beverage calories.

**Intervention:** Low-calorie sweetener (LCS) beverage (fruit-flavored Kool-Aid; 1.25-1.75 L/d depending on baseline body weight)

- Saccharin-sweetened, n=29
- Aspartame-sweetened, n=30
- RebA-sweetened, n=28
- Sucralose-sweetened, n=28

**Comparator:** Sucrose-sweetened beverage (fruit-flavored Kool-Aid; 1.25-1.75 L/d depending on baseline body weight), n=39

Other interventions: N/A

**Intervention duration:** 12wk

**Intervention compliance:** urinary PABA recovery: sucrose 63%, saccharin 72%, aspartame 72%, rebA 70%, sucralose 83% (difference between groups, P=0.37)

**Study beverage intake:**

- Habitual consumption of low-calorie sweeteners:  $\leq 1$  time/wk

**Outcome assessment methods/timing:**

- At baseline, and every 2wk until 12wk
- Weight and total body water measured using Tanita Body Composition Analyzer
- Height measured with Holtain stadiometer at baseline
- Body composition (total fat mass, total fat-free mass, total tissue percentage fat, android fat mass, and gynoid fat mass) measured using DXA at baseline and at week 12

**\* Results for total tissue percentage fat, android fat mass, gynoid fat mass, and total body water available in the paper.**

**Weight**, kg, Linear regression, Mean (SE)

**Change within group:** From 0wk-12wk

Sucrose (n=39): 1.85 (0.36), **P<0.001**

Saccharin (n=29): 1.18 (0.36), **P=0.02**

Aspartame (n=30): 0.73 (0.35), P $\geq$ 0.07

RebA (n=28): 0.60 (0.36), P $\geq$ 0.07

Sucralose (n=28): -0.78 (0.36), P $\geq$ 0.07

**Change over 12wk, compared to**

**Sucrose:**

Sucrose vs. Saccharin: P=0.21

**Sucrose>Aspartame (P<0.02), RebA**

**(P<0.02), Sucralose (P<0.001)**

**Among LCS: Sucralose<Sacch**

**(P<0.001), Asp (P=0.003), RebA**

**(P=0.008)**

**BMI**, kg/m<sup>2</sup>, Linear regression, Mean (SE)

**Change within group:** From 0wk-12wk

Sucrose (n=39): 0.62 (0.12), **P $\leq$ 0.04**

Saccharin (n=29): 0.41 (0.12), **P $\leq$ 0.04**

Aspartame (n=30): 0.22 (0.12), P $\geq$ 0.07

RebA (n=28): 0.20 (0.12), P $\geq$ 0.07

Sucralose (n=28): -0.27 (0.12), P $\geq$ 0.07

**Change over 12wk, compared to**

**Sucrose:**

Sucrose vs. Saccharin: P=NS

**Sucrose>Aspartame (P<0.05), RebA**

**(P<0.05), Sucralose (P<0.05)**

**Among LCS: Sucralose<Sacch (P<0.05),**

**Asp (P<0.05), RebA (P<0.05)**

**Total Fat Mass**, kg, Mean (SE)

**Change within group:** From 0wk-12wk

Sucrose (n=39): 1.35 (0.25), **P<0.001**

Saccharin (n=29): 0.48 (0.23), P=NS

Aspartame (n=30): 0.49 (0.23), P=NS

RebA (n=28): 0.09 (0.23), P=NS

Sucralose (n=28): -0.31 (0.24), P=NS

**Change over 12wk, compared to**

**Sucrose:**

**Sucrose>Saccharin, Aspartame, RebA**

**Sucralose, P<0.05**

**Among LCS: Sucralose<Sacch, Asp,**

**P<0.05; Saccharine, Aspartame, RebA,**

**P>0.05; RebA, Sucralose, P>0.05**

**Total Fat-Free Mass**, kg, Mean (SE)

**Change within group:** From 0wk-12wk

Sucrose (n=39): 0.84 (0.20), **P=0.001**

Saccharin (n=29): 0.70 (0.18), **P=0.006**

Aspartame (n=30): 0.63 (0.18), **P=0.01**

RebA (n=28): 0.25 (0.18), P=NS

Sucralose (n=28): -0.33 (0.19), P=NS

**TEI adjusted:** No (not in model; P $\geq$ 0.11 at baseline between treatments)

**Energy Intake, kcal/d, Mean (SD)**

**Change over 12wk, within group:**

Sucrose: increased, **P=0.007** (from bev)

Saccharin: NS

Aspartame: NS

RebA: NS

Sucralose: decreased, **P=0.02**

**Change over 12wk, compared to**

**Sucrose: Sucrose>Sacch, RebA,**

**Sucralose, P $\leq$ 0.004; Sucrose, Asp,**

**P>0.05**

**Among LCS: NS**

**Confounders accounted for:**

- Key confounders: sex, age, anthropometry at baseline, physical activity
- Other factors considered: none

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity, SES, smoking
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:** N/A

**Limitations:**

- Not all key confounders accounted for
- No information on allocation concealment
- No information on non-completers
- Trial registry did not contain data analysis plan

**Funding Source:**

USDA

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
		<p>Change over 12wk, compared to Sucrose:</p> <p>Sucrose vs Saccharin, Aspartame, <math>P&gt;0.05</math></p> <p><b>Sucrose&gt;RebA, <math>P=0.03</math>, Sucralose, <math>P&lt;0.001</math></b></p> <p><b>Among LCS: Sucralose&lt;Sacch, Asp, RebA, <math>P&lt;0.05</math>; Sacch, Asp, RebA, <math>P&gt;0.05</math></b></p>	

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Maersk, 2012</b><sup>120</sup>  <b>RCT, Denmark</b>  Baseline N=60, Analytic N=47 (Attrition: 22%); Power: NR</p> <p><b>Recruitment:</b> NR</p> <p><b>Participant characteristics: adults with overweight and obesity</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 72%</li> <li>Age: ~39y (Range 20-50y)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI ~32 kg/m<sup>2</sup> (Range 26-40)</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In overweight adults and those with obesity, drinking sucrose-sweetened cola (1 L/d) compared to aspartame-sweetened cola (1 L/d) for 6 months did not significantly affect weight, total fat mass, or lean mass. There was no difference in energy intake between groups during the intervention.</p>	<p><b>Intervention:</b> Sucrose-sweetened soft drink (SSSD; Coca Cola; 1 L/d), n=10</p> <p><b>Comparator:</b> Aspartame-sweetened diet cola (diet Coca Cola; 1 L/d), n=12</p> <p>Other interventions: milk, water</p> <p><u>Intervention duration:</u> 6mo</p> <p><u>Intervention compliance:</u> empty bottles or cartons every 3-4wk; compliance NR</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Mean SSSD at baseline: 184 mL/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 6mo follow-up</li> <li>Weight: method NR</li> <li>Total fat mass and lean body mass determined by DXA</li> </ul>	<p><b>Weight</b>, kg, ANOVA, Mean (SEM)  <b>Change over time, between groups:</b>  Diet Cola: 0.114 (1.1)  SSSD: 1.28 (1.1)</p> <p><b>Total fat mass</b>, kg, ANOVA, Mean (SEM)  <b>Change over time, between groups:</b>  Diet Cola: -0.52 (2.5)  SSSD: 3.14 (2.7)</p> <p><b>Lean mass</b>, kg, ANOVA, Mean (SEM)  <b>Change over time, between groups:</b>  Water: 0.951 (0.8)  SSSD: 0.423 (0.8)</p> <p><b><u>Data are also provided on subcutaneous abdominal adipose tissue (SAAT), visceral adipose tissue (VAT), and the ratio of the two; but none were significant for the exposures of interest.</u></b></p>	<p><b>TEI adjusted:</b> Yes (Between-group differences NS at baseline and during study)  <b>Change in EI between groups:</b>  Data NR, P=0.3</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity (NS at baseline)</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Bone mass, blood pressure, metabolic factors (leptin, cholesterol, triglycerides, fasting plasma glucose, fasting plasma insulin, HOMA-IR)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Randomization and allocation methods NR</li> <li>Baseline imbalances between groups</li> <li>No power calculation and likely underpowered</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding Sources:</b>  Danish Council for Strategic Research; The Food Study Group/Danish Ministry of Food, Agriculture and Fisheries; Novo Nordic Foundation; Clinical Institute at Aarhus University, Denmark; Danish Dairy Company, Arla Foods</p>



**Tate, 2012**<sup>133</sup>

**RCT, Choose Healthy Options  
Consciously Everyday (CHOICE), US**

Baseline N=318, Analytic N= 272;  
Attrition: 15% (ITT, n=318); Power: With  
100 participants per arm and a set at  
0.05, we had 90% power to detect a  
difference of 1.8 kg with an SD of 3.4 kg  
and 25% attrition

**Recruitment:** clinic

**Participant characteristics:  
overweight/obese adults who  
consume ≥280 kcal/d of caloric bevs**

- Total energy intake: NR
- Sex (female): 84%
- Age: 42 (10.7)y (Range 18-65y)
- Race/ethnicity: 54% black, 40% white, and 6% other
- SES: college graduate or beyond ~55%
- Anthropometrics: BMI ~36.3 (Range 25-49.9)
- Physical activity: NR
- Smoking: 9% current smoker

**Summary of findings:**

After a 6-month intervention in  
overweight and obese adults, there was  
no significant difference in weight loss or  
waist circumference between participants  
who were encouraged to substitute diet  
beverages for caloric beverages and  
those in the “attention control” group.  
Those who substituted diet beverages for  
caloric beverages were significantly more  
likely to achieve 5% weight loss  
compared to the “attention control”  
group.

**Intervention (Diet bevs, n=105):**

encouraged to replace ≥2 servings (≥200  
kcal) per day of caloric beverages with  
diet beverages; could choose any  
combination of noncaloric sweetened  
beverages of their choice (carbonated,  
noncarbonated, noncaffeinated, and  
caffeinated beverages) which were  
provided at monthly group meetings

**Comparator: “Attention Control” (AC,**  
n=105) equal treatment contact time and  
attention, monthly group sessions and  
weigh-ins, weekly monitoring; AC group  
given general weight-loss information (eg,  
instructed to read product labels, increase  
vegetable consumption, control portions,  
and increase physical activity); they were  
not given weight-loss calorie-reduction or  
physical activity goals. They were not  
encouraged to change beverage intake  
(beverages were not mentioned during the  
lessons or group sessions) and were not  
provided with beverages.

2<sup>nd</sup> Intervention Group: (Water, n=108)  
Intervention duration: 6 mo  
Intervention compliance: DB and Water  
groups consumed fewer beverage  
calories than control group at 3mo & 6mo

**Study beverage intake (kcal):** 0, 3, 6mo

**Control:** 329.3 (280.2, 378.4) 216.5  
(183.0, 249.9) 222.6 (190.6, 254.7,  
P<0.0001

**Diet bev:** 390.4 (336.8, 444.1) 119.3  
(93.4, 145.2) 130.6 (103.5, 157.6),  
P<0.0001; Group\*time: P<0.0001, Vs.  
Control: P<0.0001

**Outcome assessment methods/timing:**

- At baseline, 3mo, 6mo
- Weight measured after 12h fast using  
digital scale
- Height measured using stadiometer  
at baseline
- Waist circumference measured at the  
iliac crest

**Weight,** kg, within group, over time:  
baseline, 3mo, 6mo, mean (95% CI)

**Control:** 102.6 (99.1, 106.1), 101.1 (97.7,  
104.6), 100.7 (97.2, 104.2), P<0.0001

**Diet bevs:** 100.9 (97.1, 104.7), 99.0 (95.3,  
102.7), 98.3 (94.5, 102.1), P<0.0001

**Between group:** NS

**Likelihood of achieving 5% weight loss:**

OR (95% CI)

Control: (ref)

**Diet bevs: 2.29 (1.05, 5.01), P=0.004**

**Waist circumference,** cm, within group,  
over time: baseline, 3mo, 6mo, mean (95%  
CI)

**Control:** 116.5 (113.9, 119.2), 116.8  
(114.1, 119.5), 115.9 (113.2, 118.7),  
P=0.0107

**Diet bevs:** 115.5 (112.5, 118.5), 114.9  
(112.0, 117.8), 113.4 (110.5, 116.4),  
P=0.0103

**Between group:** NS

**TEI adjusted:** No

**Food Energy Intake, kcal/d over time:**  
**baseline, 3mo, 6mo, mean (95% CI)**

**Control:** 1861.6 (1703.8, 2019.4), 1501.5  
(1391.4, 1611.5), 1386.9 (1287.2,  
1486.6), P<0.0001

**Diet bevs:** 1886.9 (1752.1, 2021.8),  
1621.3 (1512.0, 1730.7), 1487.6 (1382.7,  
1592.5), P<0.0001; Vs. control: P<0.0001

**Water:** 1715.5 (1605.9, 1825.1), 1396.9  
(1317.6, 1476.2), 1371.1 (1253.4,  
1488.7), P<0.0001; Vs. Control: P<0.0001

**Confounders accounted for:**

- Key confounders: sex, age,  
race/ethnicity, SES, anthropometry at  
baseline, physical activity, smoking
- Other factors considered:  
medications

**Confounders NOT accounted for:**

- Key confounders: N/A
- Other factors considered: total energy  
intake, timing, temporal use, sugar,  
protein, fiber, energy density,  
supplements, alcohol

**Additional model adjustments:** N/A

**Limitations:**

- Amount of carbonated and/or  
caffeinated versions of beverages  
was not taken into account
- Trial registry did not include data  
analysis plan

**Funding Sources:**

Nestle´ Waters USA



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Vazquez-Duran, 2016<sup>137</sup></b>  <b>RCT, Clinical Trial, Mexico</b>            Baseline N=148, Analytic N=146 (Attrition: 1%); Power: a sample size of 31, which was increased by 20% loss to follow up, gave a total of 37 patients in each group. <math>\alpha=0.05</math>, <math>\beta=80\%</math> to detect -1.6% change in BMI in intervention group with SD 0.8</p> <p><b>Recruitment:</b> María Elena Maza Brito School of Nursing in Mexico City</p> <p><b>Participant characteristics: young adults consuming <math>\geq 12</math> oz/d SSB</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 81%</li> <li>Age: 21.99 (0.25) y</li> <li>Race/ethnicity: NR</li> <li>SES: all nursing students</li> <li>Anthropometrics: BMI: 26.24 (0.36) kg/m<sup>2</sup>; Overweight: 45%; Obesity: 16%</li> <li>Physical activity: &lt;1hr/d of vigorous physical activity (inclusion criteria)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            In young adults with habitual SSB intake <math>\geq 12</math> oz/d, drinking their usual consumption of caloric and non-caloric beverages compared to participants who only drank beverages with non-caloric sweeteners for 6 mo did not result in changes in BMI, waist circumference, hip circumference, phase angle (measure of body composition), and resistance/height (also a measure of composition).</p>	<p><b>Intervention:</b>            Only beverages with non-caloric sweeteners allowed (including plain water, lemon and hibiscus flavored water, coffee and tea without sugar), n=50</p> <p><b>Comparator:</b> Usual intake, n=49</p> <p>Other interventions: (2<sup>nd</sup> intervention group) No sweetened beverages permitted (only plain water, lemon and hibiscus flavored water, coffee and tea without sugar), n=49</p> <p><u>Intervention duration:</u> 6mo</p> <p><u>Intervention compliance:</u> 24hr food record 1x/week for full 6-month intervention</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Habitual SSB intake: <math>\geq 12</math> oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 3mo and 6mo follow-up</li> <li>Weight and height measured according to anthropometric standardization reference manual</li> <li>Body composition (resistance/height and phase angle) evaluated by bioelectric impedance analysis</li> <li>Waist, hip, and arm circumferences evaluated according to the anthropometric reference manual</li> </ul>	<p>All Linear regression, Mean (SD)  <b>BMI % of change</b>  <b>Change over time, within group:</b> 3mo, 6mo            ASB: -0.61 (0.08), 0.11 (0.06)            SSB (Control): 0.54 (0.06), 0.57 (0.07)  <b>Change over time, between groups:</b> 6mo            P=NS</p> <p><b>Waist Circumference % of change</b>  <b>Change over time, within group:</b> 3mo, 6mo            ASB: -1.56 (0.46), -1.23 (0.58)            SSB (Control): 0.53 (0.16), 0.62 (0.60)  <b>Change over time, between groups:</b> 6mo            P=NS</p> <p><b>Hip Circumference % of change</b>  <b>Change over time, within group:</b> 3mo, 6mo            ASB: -0.71 (0.35), -0.35 (0.46)            SSB (Control): 0.33 (0.27), 0.51 (0.31)  <b>Change over time, between groups:</b> 6mo            P=NS</p> <p><b>Resistance/Height % of change</b>  <b>Change over time, within group:</b> 3mo, 6mo            ASB: -0.85 (1.49), 2.00 (1.38)            SSB (Control): -0.43 (1.83), 0.34 (0.62)  <b>Change over time, between groups:</b> 6mo            P=NS</p> <p><b>Phase angle % of change</b>  <b>Change over time, within group:</b> 3mo, 6mo            ASB: 5.57 (1.20), 4.92 (1.28)            SSB (Control): 3.02 (0.70), 3.58 (0.96)  <b>Change over time, between groups:</b> 6mo            P=NS</p>	<p><b>TEI adjusted:</b> Yes (all participants were on individualized isocaloric diets)</p> <p><b>Energy Intake, % change from baseline EI, Mean (SD)</b>  <b>EI, change over 6mo within group:</b>            No SSB: -16.88 (2068)            Control: -6.92 (3.46)  <b>Change over time, between groups:</b>            P=0.01</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: (No baseline differences) sex, age, anthropometry at baseline</li> <li>Other factors considered: total energy intake, medications</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> </ul> <p><b>Funding Sources:</b>            Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<b>PROSPECTIVE COHORT STUDIES</b>			
<p><b>Tucker, 2015</b><sup>136</sup></p> <p><b>Prospective Cohort Study, United States</b></p> <p>Baseline N=228, Analytic N=170 (Attrition: 25%); Power: 170 participants produced statistical power of .92 to detect an effect size of .3 with participants divided into four groups and <math>\alpha = 0.05</math>.</p> <p><b>Recruitment:</b> ~20 cities in Utah and Wyoming using newspaper ads, e-mails, flyers, and word of mouth</p> <p><b>Participant characteristics: healthy women</b></p> <ul style="list-style-type: none"> <li>Total energy intake: 2017 (324) kcal/d</li> <li>Sex (female): 100%</li> <li>Age: 41.5 (3.0) y; Range 35-45y</li> <li>Race/ethnicity: ~90% non-Hispanic white</li> <li>SES: 31% Some college education, 82% Married</li> <li>Anthropometrics: NR</li> <li>Physical activity: 2581611 (823095) activity counts on accelerometer</li> <li>Smoking: 100% nonsmokers (inclusion criteria)</li> </ul> <p><b>Summary of findings:</b></p> <p>In women, sugar-sweetened soft drink intake was significantly associated with increased body weight compared to artificially sweetened soft drink intake or no soft drink intake at 4y follow-up.</p>	<p><b>Exposure of interest:</b> Sugar-sweetened soft drink intake (12-oz serving)</p> <p><b>Comparators:</b> Type of soft drink typically consumed (categorical):</p> <ul style="list-style-type: none"> <li>None</li> <li>Artificially sweetened</li> <li>Mixed (sugar and artificially sweetened)</li> </ul> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Six questions on frequency, type, and size of soft drink intake; represents weekly consumption</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Soft drink intake (12-oz serving): <ul style="list-style-type: none"> <li>&lt;0.5/wk: 36%</li> </ul> Of regular consumers: <ul style="list-style-type: none"> <li>0.5-1/wk: 55.7%</li> <li>2-6/wk: 25.3%</li> <li>≥7/wk: 19%</li> </ul> </li> <li>40.5% primarily consumed sugar-sweetened soft drinks</li> <li>41.8% primarily consumed artificially sweetened soft drinks</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 4y follow-up</li> <li>Weight measured to the nearest 0.05 kg using computerized electronic scale; all participants used restroom before being weighed, wore lightweight nylon swimsuit issued by lab, and were instructed not to eat 3hr prior</li> </ul>	<p><b>Weight</b>, kg, Change per type of soft drink consumed, Multiple regression, <math>\beta</math> (SE)</p> <p><b>TEI unadj:</b></p> <p><i>Sugar-sweetened vs Artificially-sweetened:</i>  <b>2.68 (5.14) vs -0.05 (4.40), <math>P &lt; 0.05</math></b></p> <p><i>Sugar-sweetened vs No soft drinks:</i>  <b>2.68 (5.14) vs 0.50 (5.05), <math>P &lt; 0.05</math></b></p> <p><i>Sugar-sweetened vs Mixed soft drinks:</i>  2.68 (5.14) vs 1.22 (5.06), NS</p> <p><b>TEI adjusted:</b> "relationship between soft drink consumption and changes in body weight was weakened by 28% and was no longer statistically significant" <math>P = 0.051</math></p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b></p> <p>Menopause status</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 25% without information on non-completers</li> <li>Exposure data collection tool not validated</li> <li>Exposure only measured at baseline</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>NR</p>

**Table 25. Risk of bias for randomized controlled trials examining SSB consumption versus LNCSB and growth, size, body composition and risk of overweight and obesity in adults<sup>lii, liii</sup>**

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Campos, 2015 <sup>92</sup>	Some Concerns	Low	Some Concerns	Low	Some Concerns
Higgins, 2019 <sup>108</sup>	Some Concerns	Low	Low	Low	Some Concerns
Maersk, 2012 <sup>120</sup>	High	Some Concerns	Some Concerns	Low	Some Concerns
Tate, 2012 <sup>133</sup>	Low	Low	Low	Low	Some Concerns
Vazquez-Duran, 2016 <sup>137</sup>	Low	Low	Low	Low	Low

<sup>lii</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>liii</sup> Possible ratings of low, some concerns, or high determined using the "[Cochrane Risk-of-bias 2.0](#)" (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). *Cochrane Methods. Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). [dx.doi.org/10.1002/14651858.CD201601](https://doi.org/10.1002/14651858.CD201601).)

**Table 26. Risk of bias for the prospective cohort study examining SSB consumption versus LNCSB and growth, size, body composition and risk of overweight and obesity in adults<sup>liv, lv</sup>**

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Tucker, 2015 <sup>136</sup>	Serious	Low	Moderate	Moderate	Moderate	Low	Moderate

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<sup>liv</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>lv</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

## BEVERAGE: LOW- AND NO-CALORIE SWEETENED BEVERAGES (LNCSB)

What is the relationship between beverage consumption (low and no-calorie sweetened beverages) and growth, size, body composition, and risk of overweight and obesity?

### Conclusion statements and grades

Limited evidence suggests no association between low and no-calorie sweetened beverages consumption and adiposity in children. (Grade: Limited)

Limited evidence suggests that low and no-calorie sweetened beverages consumption is associated with reduced adiposity in adults. (Grade: Limited)

### Summary of the evidence

- 37 studies identified through literature search from January 2000 to June 2019 were included in this systematic review, which examined the relationship between low and no-calorie sweetened beverages (LNCSB) and outcomes related to growth, size, body composition, and risk of overweight and obesity.<sup>1,2,7,9,11,15,22,26,27,33,41-43,46,55,62,68,103,104,106,116,118,119,127,131,137,142-152</sup>
  - Of the 17 papers in children, all were prospective cohort studies.
  - Of the 20 papers in adults, 6 were from RCTs and 14 were from prospective cohort studies.
- In studies examining LNCSB intake in children, the majority of studies (~75%) reported no association for the main outcome measure(s) of adiposity among the study populations. The remaining studies had mixed associations and methodologic concerns.
  - 3 papers with findings of increased adiposity measures
  - 1 paper with findings of decreased adiposity measures
  - 1 paper only reported height-related outcomes
- The body of evidence from children had several limitations
  - Inadequate adjustment for confounders
  - Inconsistency in methods for assessing beverage intake
  - Short study duration
  - High attrition
- In studies examining LNCSB intake in adults, the majority of studies (72%) reported a significant effect or association between LNCSB intake and adiposity; however, this was not always consistent within studies that reported multiple outcome measures.
  - One well-designed RCT and two large prospective cohort studies reported an association between LNCSB and reduced adiposity.
- The body of evidence from adults had several limitations
  - Experimental studies: short study duration, no assessment of compliance, and difference in comparators
  - Cohort studies: confounding, difference in assessment methods, poor generalizability, and high attrition

### Description of the evidence

Of the 152 articles in this systematic review, there were 37 included articles that address the

relationship between LNCSB consumption and outcomes related to growth, size, body composition, and risk of overweight and obesity. The comparator was defined as a different amount (including no intake) of the same beverage type, water, or the solid form of the beverage type (e.g., drinking apple juice compared to eating an apple). The search range included peer-reviewed articles published from January 2000 to June 2019. Studies were included if they were conducted in countries categorized as high or very high on the Human Development Index. Studies with the following designs were included: RCTs, non-randomized controlled trials (NRCTs), prospective and retrospective cohort studies, nested case-control studies, and Mendelian Randomization. Studies were included if the study participants were generally healthy or at risk for chronic disease. Participants 2 years and above were included. The studies in children and in adults were reviewed and synthesized independently.

#### *Study designs:*

- Children: 17 articles (**Table 27**)
  - Prospective cohort studies: 17 articles
- Adults: 20 articles (**Table 29**)
  - RCTs: 6 articles
  - Prospective cohort studies: 14 articles

## **LNCSB: Children**

### ***Population***

For the literature on children, mean baseline age ranged from 2 to 16 years old; seven studies had a mean baseline age of 5 years and younger.<sup>2,27,33,41,43,62,119</sup> There was a good distribution of studies by age such that these studies were representative of youth, including young children and adolescents. Lengths of follow-up were variable, ranging from 6 months to 12 years. The majority of the studies were from the United States; however, several other high or very high HDI countries were represented: Australia, Denmark, and the UK. Based on data from studies that reported race/ethnicity, most participants were primarily white; however, one study was done in Hispanics adolescents,<sup>143</sup> and three studies had other racial representation.<sup>26,55,146</sup> Analytic sample sizes ranged from 49 to 11,654. The majority of the studies did not have recruitment criteria for weight status, although one study recruited normal weight participants only<sup>62</sup> and one study recruited participants with overweight or obesity.<sup>143</sup>

### ***Intervention/exposure and comparator***

For children, all papers were observational studies. Most studies compared different levels of LNCSB, although some studies assessed different levels of LNCSB (i.e., included beverages other than just LNCSB). Two articles from the same cohort combined water and other sugar-free beverage intake as the exposure of interest.<sup>2,41</sup>

### ***Outcomes***

To discern 'healthy growth' from 'excessive growth' in children, weight status (prevalence or incidence of overweight or obesity), BMI and BMI z-scores, and body composition measures such as waist circumference and body fat, were considered to reflect "adiposity". To assess 'healthy growth' in children, outcomes such as height and lean mass were considered.

The most commonly (n=20) reported outcomes were BMI-related outcomes, including BMI, BMI

z-score, weight, and incidence of overweight or obesity. Fewer papers (n=6) reported body composition measures such as waist circumference or body fat percentage, etc. There was one study that *only* reported height-related outcomes.<sup>2</sup>

### ***Evidence synthesis***

To understand the relationship between LNCSB intake on adiposity in children, the studies that included outcomes related to weight status, BMI, body fat, and waist circumference were considered. The reviewed literature consisted of 17 observational studies, and no randomized studies. There were 16 studies that measured adiposity, and one study that measured height.

Three cohort studies reported results on the incidence or prevalence of overweight or obesity. One study found that, in adolescent girls, greater baseline intake of LNCSB was associated with greater odds of overweight and incident overweight 5 years later; however, there was no association with change in take for either overweight or incident overweight.<sup>26</sup> In adolescent boys, baseline intake of LNCSB was not associated with either overweight or incident overweight 5 years later; however, a greater increase in intake of LNCSB was significantly associated with overweight after 5 years, but not with incident overweight. Another study found that consuming LNCSB one to six times a week at age 4-5 years was significantly associated with greater risk of obesity compared with no consumption at age 7-8 years; however, this did not follow a linear pattern and there was no association between LNCSB intake at age 4-5 years and risk of overweight at age 7-8 years.<sup>119</sup> The third study found that, in school-aged children (mean age 11 years), baseline intake of LNCSB was not associated with obesity, but increased consumption was negatively associated with obesity 19 months later.<sup>146</sup>

Eight cohort studies reported results on BMI. Seven studies reported no significant association between LNCSB intake and BMI; three of which had analytic sample sizes less than 1000 participants,<sup>27,116,146</sup> three with sample sizes between 1000-2500 participants,<sup>43,55,119</sup> and one large cohort (n>10000) that looked at change in BMI over 1 year in children aged 9-14 years.<sup>7</sup> One study found that higher LNCSB intake at baseline was associated with increases in BMI in adolescent girls and boys.<sup>103</sup> In boys, increasing the amount of LNCSB consumed over time was also associated with higher BMI scores; however, this was not the case for girls.

Six cohort studies reported results on BMI z-scores. Three studies reported no significant association between LNCSB intake and BMI z-scores, and all had analytic sample sizes under 200 participants.<sup>11,33,143</sup> Two studies found a positive association between LNCSB intake and BMI z-scores; however, one study looked at the substitution of SSB with LNCSB<sup>62</sup> and another study looked at water and other sugar-free beverages as a combined exposure.<sup>41</sup> One study found that LNCSB consumption at 8 years of age was significantly associated with decreases in BMI z-scores at 11.5 years of age, when total energy intake was both adjusted and unadjusted for in the model.<sup>1</sup>

Five cohort studies reported results on body composition. Two studies reported no significant association between LNCSB intake and body composition.<sup>33,116</sup> One study with an analytic sample size less than 100 participants found no association between diet soda intake from 3-5 years of age with waist circumference at 5-6 years of age,<sup>33</sup> and one study with a sample size less than 1000 found no association with changes in percent body fat in adolescents.<sup>116</sup> Davis et al<sup>143</sup> found a significant association between LNCSB intake and increased total body fat levels in Hispanic adolescents with overweight or obesity, but no significant association with trunk fat or body fat percentage. Hasnain et al<sup>27</sup> found that greater unsweetened/diet beverage intake at 3-5

years of age was associated with greater cumulative sum of skinfolds at 15-17 years of age; however, they did not report effect magnitude and did not find a significant association with body fat percentage. Zheng et al<sup>1</sup> found that LNCSB consumption at 8 years of age was associated with decreases in body fat percentage at 11.5 years of age when total energy intake was adjusted for, but this was not significant when total energy intake was not adjusted for.

One cohort study reported results on height, and found a significant association between water plus other sugar-free beverage intake and increased height.<sup>2</sup>

Based on these studies, there is limited evidence to support an association between LNCSB intake and adiposity in children.

Energy intake is an important covariate when interpreting studies on the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity because beverages might displace nutrient-dense foods or add additional energy to the diet. Therefore, findings with and without adjustments for energy intake were extracted and reviewed. Conclusion statements reflect the totality and strength of the evidence considering both approaches. Also, funding sources were documented during data extraction for consideration when reviewing this evidence. Further, publication bias is always a consideration; however, it is not a serious concern for this body of evidence because multiple studies reported only non-significant findings while others reported significant findings or a mix of significant and non-significant.

### **Assessment of the evidence**<sup>lvi</sup>

The conclusion statement “evidence suggests no association between the intake of LNCSB and measure of adiposity among children and adolescents” was assigned a grade of **limited**. This conclusion statement is supported by 17 prospective cohort studies. As outlined and described below, the body of evidence examining LNCSB consumption and growth, size, body composition, and risk of overweight and obesity in children was assessed for the following elements when grading the strength of evidence.

**Consistency:** In terms of significantly positive or negative associations, many studies were limited to subgroup analyses or modeling exercises in studies without pre-specified analysis plans, and in most cases these findings were not consistent with the overall findings for the entire study population or for the primary outcome. However, there were enough studies, and reasonably consistent findings (primarily of no association), to support a limited evidence recommendation.

**Directness:** Most studies were designed to directly measure and analyze the relationship between LNCSB intake and outcomes related to growth, size, and body composition. Only one study group compared LNCSB with water. The population, intervention/exposure, comparators, and outcomes (PICO elements) of the body of evidence align with the PICO elements outlined a priori in the Analytic Framework.

**Precision:** There is a moderate degree of certainty around an effect estimate for adiposity. Five

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<sup>lvi</sup> A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.



studies had sample sizes less than 200 participants, and several studies did not report effect size or confidence intervals.

**Generalizability:** The majority (76%) of studies were conducted in the United States. There was a good distribution of age ranges across young children and adolescents, with mean baseline ages ranging from 2 to 16 years old.

**Risk of bias:** There were no randomized studies. None of the observational studies accounted for all key confounders (see **Table 28**). Other domains of concern were classification of exposures, missing data (very high attrition for several studies ranging from 47-80%), and selection of reported results.

## **LNCSB: Adults**

### ***Population***

For the literature on adults, mean baseline age ranged from 25 to 69 years old with follow-up times ranging from 2 years to 20 years. The majority of the studies were from the United States; however, several other high or very high HDI countries were represented: Australia, Denmark, France, Iran, Mexico, and Spain. Based on data from studies that reported race/ethnicity, most participants were primarily white; however, one RCT had other racial representation,<sup>150,151</sup> as did four observational studies.<sup>104,131,144,149</sup> There were several large cohorts, with a range of analytic sample sizes from 50 to 52,987. The majority of studies did not have recruitment criteria for weight status; however, four RCTs recruited women with overweight and obesity.<sup>147,148,150,151</sup>

Data from some cohorts and controlled trials were reported in more than one publication. These articles were included if the outcomes differed thus providing new data. The cohorts analyzed and reported in multiple publications include: Health Professionals Follow-Up Study (HPFS),<sup>42,46,127</sup> Nurses' Health Study (NHS),<sup>42,46,127</sup> and Nurses' Health Study II.<sup>9,42,46,152</sup> There were data from 2 RCTs that were each reported in 2 papers.<sup>147,148,150,151</sup>

### ***Intervention/exposure and comparator***

For adults, observational studies included either a continuous or a categorical measure of LNCSB intake as the intervention or exposure, where intake represents a combination of different levels of LNCSB consumption and/or LNCSB (i.e., including beverages other than just LNCS soda). In the RCTs, LNCSBs as the intervention was compared to either no LNCSB or usual (low level) intake. One RCT was a crossover trial in which participants consumed 660 mL daily of LNCSB or carbonated water for 12 weeks in each arm.<sup>142</sup> Another RCT was a 24-week weight loss trial with a 1-year maintenance phase conducted in overweight or obese women who were habitual consumers of diet beverages; one group of participants continued their usual LNCSB intake by drinking 250 mL after lunch 5 days a week, and another group substituted 250 mL water for LNCSB.<sup>147,148</sup> Vazquez-Duran et al<sup>137</sup> conducted an RCT in which Mexican nursing students were divided into three arms of using LNCSB, SSB or no intervention for 6 months. For LNCSB, the intervention group was permitted to drink only beverages with LNCS, and the comparator group was not permitted to drink sweetened beverages. The final RCT was a 12-week weight loss trial with a 40-week maintenance phase conducted in adults with overweight or obesity with habitual intake of LNCSB.<sup>150,151</sup> In this study, the intervention group consumed at least 24 fluid ounces (710 ml) daily of LNCSB, with unrestricted water consumption; the comparator group consumed at least 24 fluid ounces (710 ml) daily of water and refrained from LNCSB consumption.

## **Outcomes**

In adults, weight status (prevalence or incidence of overweight or obesity), BMI, and body composition measures such as waist circumference, body fat, and abdominal adiposity were considered to reflect “adiposity”.

In adults, outcomes include weight, weight status, BMI, and body composition. The most commonly reported outcomes were weight (n=12), waist circumference (n=12), and BMI (n=7). Fewer papers (n=5) reported incidence of overweight or obesity, or other measures of body composition measures such as visceral adipose tissue, etc. There was one RCT that reported hip circumference in addition to other outcomes related to adiposity.<sup>137</sup>

## **Evidence synthesis**

The reviewed literature consisted of 14 observational studies and 6 RCTs that examined the relationship between LNCSB and adiposity outcomes in adults.

Five papers<sup>142,147,148,150,151</sup> from three RCTs and seven papers from cohort studies reported results on weight; however, the results were not consistent. Among the RCTs, the strongest trial<sup>150,151</sup> methodologically reported an inverse association between LNCSB and weight in both the 24-week weight loss phase and 53-week weight maintenance phase.<sup>150,151</sup> The weaker trial indicated a positive association between LNCSB and weight after the 12-week weight loss phase, but declining over the 40-week weight maintenance phase.<sup>147,148</sup> The final trial reported no association between LNCSB and weight.<sup>142</sup> Of the cohort studies, four papers from large cohorts found significant associations between LNCSB intake and decreased body weight; however, it is worth noting that the study included overlapping cohorts/participants.<sup>9,42,46,152</sup> Three cohort studies reported no significant association between LNCSB and weight: one study was conducted among Hispanic females in Mexico,<sup>131</sup> another had a sample size just over 1000 participants,<sup>118</sup> and one study investigated the substitution of 1 serving/day of water for LNCSB.<sup>22</sup> There was moderate evidence that LNCSB consumption was inversely associated with body weight.

Six papers from four RCTs and six prospective cohort studies reported on waist circumference. Among the RCTs, two reported no significant association between LNCSB intake and waist circumference.<sup>142,147,148</sup> One study among young adults with habitual intake of SSB found a positive association between LNCSB intake and waist circumference.<sup>137</sup> The study with the strongest methodology was a 1-year trial with 12 weeks of weight loss then maintenance, and found that LNCSB intake was significantly associated with lower waist circumference.<sup>150,151</sup> Among the six cohort studies, five reported a significant association between LNCSB intake and increased waist circumference.<sup>68,104,144,145,149</sup> Duffey et al<sup>144</sup> only measured LNCSB intake at baseline and reported on waist circumference over 20 years. Ferreira-Pego et al<sup>68</sup> assessed individuals with high risk for cardiovascular disease and reported abdominal obesity with LNCSB consumption in a high intake group of only 83 participants versus a group with intake of less than 1 serving per week. Fowler et al<sup>104</sup> reported on a trial in adults aged 65 years and older and had an analytic sample size less than 1000 participants. Hinkle et al<sup>145</sup> evaluated data from women with a history of gestational diabetes. Nettleton et al<sup>149</sup> had questionable data on total energy intake and did not find a positive association after adjusting for baseline waist circumference). One study found an inverse association between change in daily or monthly servings of LNCSB and waist circumference; however, this study was conducted in Hispanic females where only 20% of the sample consumed LNCSB and mean intake was just 0.1 serving per week.<sup>131</sup> There was limited evidence from RCTs and weak evidence with mixed findings from observational studies

that LNCSB is not associated with increased waist circumference.

Five papers from three RCTs and five prospective cohort studies reported results on BMI. Among the RCTs, one study was a crossover trial that found no association between LNCSB and BMI.<sup>142</sup> In another RCT, the group that consumed LNCSB had lower BMI reduction compared to the group that consumed water; however, this was a weak intervention with limited power and the magnitude of the effect diminished markedly after a 12-month follow up indicating the effect was not sustainable.<sup>147,148</sup> The final RCT was conducted in Mexican nurses and found a lower reduction in BMI in the group using LNCSB versus LNCSB proscription; however, the magnitude of the intervention was not reported.<sup>137</sup> Among observational studies, three found no association between LNCSB intake and BMI. One study investigated habitual LNCSB intake during pregnancy and post-partum follow-up<sup>145</sup> and another study was designed to test the effects of SSB intake on obesity based on genetic predisposition.<sup>127</sup> Another study was a mathematical modeling study of substituting one serving/day of LNCSB with water.<sup>22</sup> Two studies found a significant association between LNCSB and BMI. One study was a small cohort (N=466) with 38% attrition in which weight was stated as the primary outcome but was not mentioned in the paper; this study reported a ~0.4 kg/m<sup>2</sup> increment in BMI over 10 years for high consumers of LNCSB (≥1 soda/day) versus none/non-users.<sup>104</sup> The second study reported higher BMI with LNCSB intake; this study dichotomized participants by frequency of LNCSB intake, measured exposure only at baseline, and reported on BMI 13 years later.<sup>106</sup>

Two prospective cohort studies reported indices of body fatness, and both found no significant association between LNCSB intake and visceral adipose tissue as a measure of body fatness.<sup>118,145</sup> There was insufficient evidence to draw conclusions regarding LNCSB intake and body fatness.

Energy intake is an important covariate when interpreting studies on the relationship between beverage consumption and growth, size, body composition, and risk of overweight and obesity because beverages might displace nutrient-dense foods or add additional energy to the diet. Therefore, findings with and without adjustments for energy intake were extracted and reviewed. Conclusion statements reflect the totality and strength of the evidence considering both approaches. Also, funding sources were documented during data extraction for consideration when reviewing this evidence. Further, publication bias is always a consideration; however, it is not a serious concern for this body of evidence because multiple studies reported only non-significant findings while others reported significant findings or a mix of significant and non-significant.

## **Assessment of the evidence**<sup>lvii</sup>

The conclusion statement “evidence suggests that LNCSB consumption is associated with reduced adiposity in adults” was assigned a grade of **limited**. The conclusion statement is supported by the 4 RCTs and 13 prospective cohort studies. As outlined and described below, the body of evidence examining LNCSB consumption and growth, size, body composition, and risk of overweight and obesity in adults was assessed for the following elements when grading

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<sup>lvii</sup> A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

the strength of evidence.

**Consistency** The majority of RCTs and cohort studies reported an association between LNCSB intake and adiposity. However, of the studies that reported multiple outcomes, few found significant associations across all reported outcomes.

**Directness:** There were limitations related to the body of evidence in adults in terms of alignment with the PICO elements determined *a priori*. Three of the four controlled trials were interventions in those with or at high risk of overweight or obesity. In Madjd et al,<sup>147,148</sup> participants were asked to replace regular consumption of diet beverages with water. In Peters et al,<sup>150,151</sup> participants were asked to consume water and refrain from non-nutritive sweetener beverages. In Vazquez-Duran et al,<sup>137</sup> the comparator group was not permitted to drink sweetened beverages.

**Precision:** The body of evidence demonstrates limited precision mostly due to small sample sizes. Samples sizes of the RCTs ranged from 29 per arm<sup>148</sup> to 158 per arm.<sup>150</sup> Four prospective cohort studies had sample sizes less than 2000 participants.

**Generalizability:** Among RCTs, the body of evidence demonstrates limited generalizability with regard to participant characteristics. Among prospective cohort studies, the body of evidence demonstrates moderate generalizability. The majority of cohort studies were conducted in the United States; however, several small cohorts had high attrition and two large cohorts were conducted among health professionals and may not be generalizable to other populations.

**Risk of bias** was considered limited for this evidence for both RCTs and cohort studies (see **Table 30** and **Table 31**). Few studies accounted for all key confounders by design or through analysis. Other domains of concern were missing data and selection of reported results.

## Research recommendations

To address the limitations of this body of evidence, several research recommendations have been identified:

- Measure beverage consumption and patterns and study their effect on human health through all life stages using more consistent and improved terms, controls, and research methods
- Compare intake of particular beverages to intake of water or another comparator
- Differentiate between LNCSB and SSB (cleanly separate the two)
- Design studies that emphasize assessments of relationships between the intakes of added sugars and low-calorie sweeteners and body weight, adiposity, and cardio-metabolic health in diverse sub-populations who are at high risk of obesity and related morbidities.

Table 27: Summary of articles examining the relationship between LNCSB consumption and growth, size, body composition and risk of overweight and obesity in children<sup>lviii</sup>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
PROSPECTIVE COHORT STUDIES			

<sup>lviii</sup> Abbreviations: adj: adjusted; ANCOVA: analysis of covariance; ANOVA: analysis of variance; ASB: artificially-sweetened beverage; BF: body fat; BMI: body mass index; BMIZ: BMI z-score; CDC: Center for Disease Control and Promotion; CI: confidence interval; d: day(s); FFQ: food frequency questionnaire; HHS: United States Department of Health and Human Services; N/A: not applicable; NCI: National Cancer Institute; NHLBI: National Heart, Lung, and Blood Institute; NICHD: National Institute of Child Health and Human Development; NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases; NIH: National Institutes of Health; NR: not reported; NS: not significant; OR: odds ratio; SD: standard deviation; SE: standard error; SES: socioeconomic status; SSB: sugar-sweetened beverage; svg: serving(s); T: tertile; TEI: total energy intake; unadj; unadjusted; USDA: U.S. Department of Agriculture; WC: waist circumference; wk: week(s); y: year(s)  
Red font indicates a statistically significant detrimental relationship, and green font indicates a statistically significant beneficial relationship.

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Berkey, 2004<sup>7</sup></b>  <b>Prospective Cohort Study, Growing Up Today Study, United States</b>  Baseline N=16771, Analytic N=11654 (Attrition: 31%); Power: NR</p> <p><b>Recruitment:</b> convenience sample (children of NHSII participants)</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Boys, Mean~2290 kcal/d; Girls, Mean~2050 kcal/d</li> <li>Sex (female): ~57%</li> <li>Age: Range: 9-14 y</li> <li>Race/ethnicity: White, 94.7%</li> <li>SES: NR</li> <li>Anthropometrics: Overweight (&gt;85<sup>th</sup> percentile CDC BMI charts): boys: 23.2%; girls: 17.5%; Very lean (&lt;10<sup>th</sup> percentile): boys: 7.2%; girls: 8.6%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  There was not a significant association between increases in diet soda servings/d and BMI change over 1y in boys or girls.</p>	<p><b>Exposure of interest:</b> Diet soda</p> <p><b>Comparator:</b> Diet soda intake (continuous; 1 y change in svg/d)</p> <p>Other exposures: milk, sugar added beverages, fruit juices</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Self-administered semi-quantitative, validated FFQ for older children and adolescents; Represents intake during previous year</li> <li>At baseline, 1y follow-up, 2y follow-up</li> </ul> <p><b>Study beverage intake:</b> svg/d</p> <ul style="list-style-type: none"> <li>Diet soda intake: <ul style="list-style-type: none"> <li>Boys: Mean~0.16</li> <li>Girls: Mean~0.18</li> </ul> </li> </ul> <p><b>Outcome assessment methods/timing:</b>  At baseline, 1y follow-up, 2y follow-up BMI from height and weight self-reported by children with measuring instructions and suggestion to ask someone for help provided (all have mothers who are nurses in NHSII)</p>	<p><b>Diet soda intake, continuous BMI change over 1y</b>, kg/m<sup>2</sup>, <math>\beta</math> (SE), Linear regression  Per 1y svg/d increase:  <b>Not adjusted for TEI</b>  Boys: 0.119 (0.068), P=0.080  Girls: 0.065 (0.048), P=0.175  <b>Adjusted for TEI</b>  Boys: 0.100 (0.070), P=0.152  Girls: 0.056 (0.048), P=0.244</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Tanner stage, menarche (girls), height growth, milk type, inactivity, other beverage intake (sugar added, diet soda, fruit juices)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Children lost to follow-up were older and had higher sugar added beverage intake and lower milk intake at baseline</li> <li>Self-reported height and weight</li> <li>Sugar-added beverage analyses differ from analyses for other beverage types</li> <li>No preregistered protocol</li> </ul> <p><b>Funding sources:</b>  NIH; Boston Obesity Nutrition Research Center Grant; CDC; Economic Research Service of the USDA; Kellogg's</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Blum, 2005<sup>11</sup></b>  <b>Prospective Cohort Study, United States</b>  Baseline N=830 Analytic N=166  (Attrition: 80%) Power: NR</p> <p><b>Recruitment:</b> convenience sample of elementary school children in grades 3 through 6 who had participated in a previous study</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean (SD): 1957.7 (575.3) kcal/d</li> <li>Sex (female): 55.4%</li> <li>Age: 9.3 (1.0) y</li> <li>Race/ethnicity: Caucasian, ~94%</li> <li>SES: NR</li> <li>Anthropometrics: BMI z-score, 0.47 (1.0); Height, 139.4 (7.9) cm; Weight, 35.7 (8.1) kg</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Children who remained in the same weight category after 2y (either normal weight or overweight), consumed significantly more diet soda compared to baseline. There was no difference in diet soda intake over time among children who changed weight categories. Change in diet soda intake did not vary by BMIZ group. Child diet soda intake was not significantly associated with BMI z-score two years later.</p>	<p><b>Exposure of interest:</b> Diet soda</p> <p><b>Comparator:</b> Diet soda intake (continuous; oz/d)</p> <p>Other exposures: milk, 100% juice, sugar sweetened drinks</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>24-hr recall with two interviews per 24-hr period; parents of random sub-sample called to verify consumption at home; Represents intake during past 24-hr</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b> oz/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>Diet soda: 0.3 (1.8)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At 2y follow-up</li> <li>BMI z-score (CDC age and gender specific) from height and weight measured once</li> </ul>	<p><u>Change in Diet soda intake for Change-in-BMIZ subgroups</u>, oz/d; ANOVA, Mean (SD):</p> <p><b>Unadjusted analysis</b></p> <p>Within group differences (t-tests):  Normal wt at baseline &amp; 2y, n=99: 1.1 (3.9), P&lt;0.05  Overweight at baseline &amp; 2y, n=48: 2.3 (7.3), P&lt;0.05  Gained wt (Normal wt at baseline; Ovwt at 2y), n=11: 3.6 (6.8), NS  Lost wt (Ovwt at baseline; Normal wt at 2y), n=6: 1.7 (4.1), NS</p> <p>Between group differences (ANOVA): All NS</p> <p><u>BMI z-score</u>, linear regression  Increase per oz/d increase in baseline intake:  P=NS, Data: NR</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>TEI, Change-in-BMIZ subgroups</b>, kcal/d; ANOVA, Mean (SD):  Within group differences:  Normal wt at baseline &amp; 2y, n=99: -118.4 (724.9), P&lt;0.05  Overweight at baseline &amp; 2y, n=48: -165.1 (693.1), NS  Gained wt (Normal wt at baseline; Ovwt at 2y), n=11: -173.6 (592.0), NS  Lost wt (Ovwt at baseline; Normal wt at 2y), n= 6: 140.3 (920), NS  Between group differences: All NS</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline,</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Baseline beverage intakes, 2y follow-up beverage intakes</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Single 24-hr recall used to assess intake</li> <li>Impact of high level of missing data on analyses unclear</li> <li>No a priori protocol to confirm analysis plan</li> </ul> <p><b>Funding source:</b>  NR</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Davis, 2018<sup>143</sup></b>  <b>Prospective Cohort Study, Study of Latino Adolescents at Risk for Diabetes (SOLAR), United States</b>            Baseline N=NR, Analytic N=98 (Attrition: NR%); Power: 80% power to detect differences in total body fat (effect size of 0.3)</p> <p><b>Recruitment:</b> from greater Los Angeles County community health clinics, health fairs, and word of mouth</p> <p><b>Participant characteristics: Hispanic adolescents with overweight or obesity</b></p> <ul style="list-style-type: none"> <li>Total energy intake: ~1800 kcal/d</li> <li>Sex (female): 44%</li> <li>Age: 14.0 (1.8) y</li> <li>Race/ethnicity: 100% Hispanic</li> <li>SES: NR</li> <li>Anthropometrics: BMI % 96.6 (4.6); 17% Overweight, 84% Obese</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            In Hispanic children with overweight or obesity, ASB intake was not significantly associated with changes in BMIZ, trunk fat, or fat percentage at 1yr follow-up. Compared to the control (no ASB intake), chronic ASB consumers and ASB initiators had increased total body fat levels at 1yr follow-up.</p>	<p><b>Exposure of interest:</b> Artificial sweetened beverages (ASBs included sodas, coffees, energy drinks, teas, sports drinks, juices, and flavored waters); 1 svg = 8 oz</p> <p><b>Comparators:</b> ASB intake (categorical):</p> <ul style="list-style-type: none"> <li>Control: No ASBs at baseline or 1yr</li> <li>ASB initiators: No ASBs at baseline but started drinking ASBs at 1yr</li> <li>Chronic ASB consumers: consumed ASBs at baseline and at 1yr</li> </ul> <p>Other exposure measures: N/A</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Two 24hr dietary recalls using multiple pass method</li> <li>At baseline, 1y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>ASB initiators: 14%               <ul style="list-style-type: none"> <li>1.75 (0.5) svg/d at 1yr</li> </ul> </li> <li>Chronic ASB consumers: 9%               <ul style="list-style-type: none"> <li>1.4 (0.8) svg/d at baseline</li> <li>1.6 (1.0) svg/d at 1yr</li> </ul> </li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 1y follow-up</li> <li>Height measured using wall-mounted stadiometer; average of two measurements used for analysis</li> <li>Weight measured using beam medical scale; average of two measurements used for analysis</li> <li>BMI z-scores (BMIZ) determined using EPII 2000 software</li> <li>Whole-body fat and soft lean tissue measured by DEXA</li> </ul>	<p><b>BMIZ</b>, ANCOVA, Mean (SD),  <b>Change at 1yr by ASB consumption:</b>            Control (n=75): 2.0 (0.6)            ASB Initiators (n=14): 2.1 (0.4)            Chronic ASB (n=9): 2.2 (0.5)            P for group effect = 0.15            P for interaction = 0.28</p> <p><b>Total fat</b>, kg, ANCOVA, Mean (SD)  <b>Change at 1yr by ASB consumption:</b>            Control (n=75): 28.9 (10.7)            ASB Initiators (n=14): 34.2 (10.2)            Chronic ASB (n=9): 34.5 (12.2)  <b>P for group effect = 0.05</b>            P for interaction = 0.96</p> <p><b>Trunk fat</b>, kg, ANCOVA, Mean (SD)  <b>Change at 1yr by ASB consumption:</b>            Control (n=75): 15.1 (6.1)            ASB Initiators (n=14): 17.2 (6.3)            Chronic ASB (n=9): 17.0 (5.9)            P for group effect = 0.22            P for interaction = 0.91</p> <p><b>Fat %</b>, ANCOVA, Mean (SD)  <b>Change at 1yr by ASB consumption:</b>            Control (n=75): 34.4 (8.3)            ASB Initiators (n=14): 37.0 (7.4)            Chronic ASB (n=9): 35.5 (7.8)            P for group effect = 0.34            P for interaction = 0.72</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, race/ethnicity</li> <li>Other factors considered: total energy intake, sugar, fiber, medications</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: age, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, protein, energy density, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>            Tanner stage</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No information on baseline N, attrition, or non-completers</li> <li>ASB consumption was rare and may have affected power</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>            NIDDK; General Clinical Research Center for Health Resources</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Dong, 2015<sup>15</sup></b>  <b>Prospective Cohort Study, Avon Longitudinal Study of Parents and Children (ALSPAC), UK</b>  Baseline N=15,444 (recruited), Analytic N=4,646 (Attrition: 70%) Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49.2%</li> <li>Age: Mean=7.5y</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI, Mean=16.2; BMI z-score, Mean=0.1</li> <li>Physical activity: Mean=22.9 min/d, SD=15.4 (at 11y)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Among children, neither average intake nor increases in intake of diet soda over 3y were significantly associated with excessive weight gain (increase in BMI z-score).</p>	<p><b>Exposure of interest:</b> Diet soda (diet fizzy drinks, diet squashes and cordials)</p> <p><b>Comparators:</b> Diet soda (continuous; g/d)</p> <ul style="list-style-type: none"> <li>Per 100 g/d change over 3y</li> <li>Per 100 g/d average across 3y</li> </ul> <p>Other exposures: full-fat milk, low-fat milk, sugar-sweetened beverages, juices</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Three-day food diary, child report with help from parent; Represents current intake</li> <li>At 7y, 10y, and 13y</li> </ul> <p><b>Study beverage intake:</b> g/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>Diet soda: <ul style="list-style-type: none"> <li>7y: 133.3 (163.8)</li> <li>10y: 101.6 (155.0)</li> <li>13y: 102.7 (175.5)</li> </ul> </li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At 7y, 10y, and 13y</li> <li>Height and weight measured by study personnel</li> <li>Calculated UK age and sex adjusted BMI z-score to represent adiposity</li> <li>Excessive weight gain: increase in adiposity over 3y compared to reference group</li> <li>BMI converted to g for interpretation (assumes 0.01 increase in BMI z-score = 50g)</li> </ul>	<p><b>Excess weight gain (g) over 3y</b>, per 100 g/d increase (change) or per 100 g/d intake (average), Mean, linear regression</p> <p><b>Diet soda intake, continuous</b>  Change: B: 10, P=NS  Average: B: 30, P=NS  <b>Boys (n=2155)</b>  Change: B: 6, P=NS  <b>Girls (n=2193)</b>  Change: B: 13, P=NS  <b>7-10y period</b>  Change: B: 25, P=NS  <b>10-13y period</b>  Change: B: 41, P=NS</p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, physical activity</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, anthropometry at baseline, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> puberty status (Tanner stage)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Impact of missing data on analyses unclear</li> <li>Results from subgroup analyses are only report for change data, not average intake data which may show fewer/no significant associations</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NR</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Field, 2014</b><sup>103</sup></p> <p><b>Prospective Cohort Study, Growing Up Today Study (GUTS) II cohort, United States</b></p> <p>Baseline N=10919; Analytic N=7559; Attrition: 31%; Power: NR</p> <p><b>Recruitment:</b> recruited by sending letters to women in the Nurses' Health Study II who had children aged 9-15 years</p> <p><b>Participant characteristics: adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 55%</li> <li>Age: ~13y (Range 9-16y)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics: BMI ~20; Overweight ~20%</li> <li>Physical activity, vigorous: ~7h/w</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In adolescents, higher diet soda intake at baseline was associated with increases in BMI in girls and boys. In boys, increasing the amount of diet soda consumed over time was also associated with higher BMI scores.</p>	<p><b>Exposure of interest:</b> Low calorie soda intake</p> <p><b>Comparators:</b> intake, continuous; svg/d</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Youth/Adolescent questionnaire; validated</li> <li>At baseline and 2y, 4y, 7y follow-up</li> </ul> <p><b>Study beverage intake:</b> NR</p> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline and 2y, 4y, 7y follow-up</li> <li>Weight and height self-reported</li> <li>BMI calculated as kg/m<sup>2</sup></li> </ul>	<p><b><u>Change in BMI with baseline intake and change in intake, <math>\beta</math> (95% CI)</u></b></p> <p>[Note: change in intake was adjusted for baseline intake in these results. Analyses looking at only baseline intake or change in intake without adjusting for baseline are presented in the paper]</p> <p><b><u>Change in BMI with baseline intake and change in intake, <math>\beta</math> (95% CI)</u></b></p> <p><b><u>GIRLS:</u></b></p> <p><b>Diet soda: 0.21 (0.07, 0.35)</b></p> <p>Change in diet: 0.04 (-0.12, 0.20)</p> <p><b><u>BOYS:</u></b></p> <p><b>Diet soda: 0.56 (0.32, 0.80)</b></p> <p><b>Change in diet: 0.45 (0.22, 0.69)</b></p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Tanner stage of development (boys only), hours per day of television viewing, time between assessments, baseline and change values for other 2 beverages of interest</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 31% without information on non-completers</li> <li>Weight and height self-reported</li> <li>Follow-up time may have varied as participants were included if they had weight data on <math>\geq 2</math> consecutive assessment points</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>Breast Cancer Research Foundation and NIH</p>

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<p><b>Haines, 2007<sup>26</sup></b>  <b>Prospective Cohort Study, Project Eating Among Teens, United States</b>  Baseline N=4746 Analytic N=2516 (Attrition: 47%) Power: NR</p> <p><b>Recruitment:</b> population based sample</p> <p><b>Participant characteristics: adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean (SD): Girls, 1994 kcal/d (1047); Boys,</li> <li>Sex (female): 55.1%</li> <li>Age, Mean (SD): Middle school cohort, 12.8 y (0.8); High school cohort, 15.8y (0.8)</li> <li>Race/ethnicity: 48.3% white, 18.9% black, 19.6% Asian, 5.8% Hispanic, 3.6% Native American, 3.8% mixed race or other</li> <li>SES: Low or low-middle SES, 37%</li> <li>Anthropometrics: BMI (Mean), Girls 22.4, Boys 22.5; Overweight (&gt;85<sup>th</sup> percentile), Girls 25.7%, Boys 26.4%</li> <li>Physical activity, Mean (SD): Girls, 5.8 h/wk (4.7); Boys,</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In adolescent girls, greater intake of diet soda was associated with greater odds of overweight and incident overweight 5 years later. In adolescent boys, a greater increase in intake of diet soda was associated with overweight after 5 years.</p>	<p><b>Exposure of interest:</b> Diet soda</p> <p><b>Comparators:</b> Diet soda (continuous; svg/d)</p> <ul style="list-style-type: none"> <li>Baseline intake</li> <li>Change in intake</li> </ul> <p>Other exposures: milk, sugar-sweetened beverages</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>149 item semi-quantitative Youth and Adolescent FFQ (YAQ); Represents usual intake</li> <li>At baseline, 5y follow-up</li> </ul> <p><b>Study beverage intake:</b> svg/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>Milk intake: <ul style="list-style-type: none"> <li>Girls: 1.4 (1.4)</li> <li>Boys: 1.9 (1.5)</li> </ul> </li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 5y follow-up</li> <li>Weight and height self-reported</li> <li>Overweight defined as BMI &gt;85<sup>th</sup> percentile for age and gender, using Must et al. classification</li> </ul>	<p><b>GIRLS:</b>  <b>Overweight at 5y follow-up</b>, OR (95% CI), Logistic Regression  Baseline intake: <b>1.74 (1.13, 2.69)</b>  Change in intake: Data NR, P=NS</p> <p><b>Incident overweight</b>, OR (95% CI), Logistic Regression  Baseline intake: <b>1.99 (1.14, 3.50)</b>  Change in intake: Data NR, P=NS</p> <p><b>BOYS:</b>  <b>Overweight at 5y follow-up</b>, OR (95% CI), Logistic Regression  Baseline intake: 1.58 (0.84, 2.99)  Change in intake: <b>Data NR, P&lt;0.05</b></p> <p><b>Incident overweight</b>, OR (95% CI), Logistic Regression  Baseline intake: 0.72 (0.21, 2.42)  Change in intake: Data NR, P=NS</p>	<p>TEI adjusted: Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> none</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Did not account for two key confounders</li> <li>Attrition 47% with no information on non-completers</li> <li>Height and weight self-reported</li> <li>No preregistered protocol to compare analyses</li> </ul> <p><b>Funding source:</b>  Maternal and Child Health Bureau (HHS)</p>

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<p><b>Hasnain, 2014<sup>27</sup></b>  <b>Prospective Cohort Study, Framingham Children's Study, United States</b>  Baseline N=106, Analytic N=98 (Attrition: 8%); Power: NR</p> <p><b>Recruitment:</b> convenience</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~1724 kcal/d</li> <li>Sex (female): 55.1%</li> <li>Age: 3-5y</li> <li>Race/ethnicity: 100% non-Hispanic white</li> <li>SES: Maternal education &gt;college, ~34%; 100% 2-parent household</li> <li>Anthropometrics: BMI, Mean~16.1</li> <li>Physical activity: Mean~10.7 Caltrac counts/hr</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  Unsweetened/diet beverage intake from 3-9y was not associated with body fat %, BMI, sum of skinfolds, or waist circumference at 15-17y, but throughout childhood greater unsweetened/diet beverage intake was associated with greater sum of skinfolds.</p>	<p><b>Exposure of interest:</b> Unsweetened/diet beverages (diet/artificially sweetened carbonated and noncarbonated beverages, unsweetened and artificially sweetened tea and coffee)</p> <p><b>Comparators:</b> Unsweetened/diet beverage intake (categorical; tertiles)</p> <ul style="list-style-type: none"> <li>T1 (Mean=0.0 oz/d, SD=0.0)</li> <li>T2 (Mean=0.4 oz/d, SD=0.2)</li> <li>T3 (Mean=2.3 oz/d, SD=1.5)</li> </ul> <p>Other exposures: milk, fruit and vegetable juice, SSBs</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Up to 4 sets of 3-d diet records annually completed by parents; Represents usual intake</li> <li>At baseline (3-5y), annually for 12y (age 15-17y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Unsweetened/diet beverages, Median (5<sup>th</sup>, 95<sup>th</sup> percentile): 0.0 oz/d (0.0, 3.3)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>End of follow-up (15-17y)</li> <li>Weight, height, waist circumference measured by study personnel</li> <li>Four skinfolds (triceps, subscapular, suprailiac, abdominal) measured in duplicate following standard protocol</li> <li>Percent body fat measured with DXA scan</li> </ul>	<p><u><b>Effects of intake (by tertile) at ages 3-9y on outcomes at end of follow-up (ages 15-17y): linear regression</b></u></p> <p><u><b>Body fat %</b></u>, Mean: Data NR, P=0.5841  <u><b>BMI</b></u>, kg/m<sup>2</sup>: Data NR, P=0.4444  <u><b>Sum of 4 skinfolds</b></u>, mm: Data NR, P=0.2713  <u><b>WC</b></u>, cm: Data NR, P=0.3959</p> <p><u><b>Effects of intake (by tertiles) on sum of skinfolds over time; mixed model</b></u></p> <p>T1 vs T2: Data NR, P=0.2525  <b>T1 vs T3: Data NR, P=0.0394</b>  T2 vs T3: Data NR, P=0.3569</p>	<p><b>TEI adjusted:</b> Evaluated but not independent predictor so removed from model</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> percent of calories from fat, mean TV and video time, other beverages consumed, maternal education, maternal BMI</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Validation of 3-d diet records not indicated</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NHLBI; National Dairy Council</p>

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<p><b>Kral, 2008<sup>33</sup></b>  <b>Prospective Cohort Study, United States</b>            Baseline N=NR, Analytic N=49 (Attrition: NR); Power: NR</p> <p><b>Recruitment:</b> convenience sample from newborn nurseries, obstetric practices, pediatric practices and local referrals</p> <p><b>Participant characteristics: children at high or low risk for obesity</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female) at age 3: ~44%</li> <li>• Age: Mean ~3 y</li> <li>• Race/ethnicity: 100% White</li> <li>• SES: NR</li> <li>• Anthropometrics at age 3: BMI z-score, Mean ~ -0.4; WC, Mean ~49.8 cm</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            Change in diet soda intake from 3 to 5y was not associated with change in BMI z-score or WC from 5 to 6y.</p>	<p><b>Exposure of interest:</b> Diet soda (carbonated noncaloric beverages)</p> <p><b>Comparator:</b> Diet soda intake (change from 3y to 5y; continuous; kcal/d)</p> <p>Other exposures: milk, fruit juice, fruit drinks, soda, soft drinks, all beverages</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Three day weighed food and beverage record (2 weekdays, 1 weekend day) recorded by primary caregiver; Represents usual intake</li> <li>• At baseline (3y), annually (4y and 5y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Diet soda: Mean ~0.03 oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, annually (4y, 5y, and 6y)</li> <li>• Waist circumference measured in triplicate at the narrowest part of torso by trained anthropometrists</li> <li>• Height and weight measured in triplicate by trained anthropometrists</li> <li>• BMI z-score calculated using CDC growth charts</li> </ul>	<p><b>BMI z-score change from 5y – 6y.</b> per change in kcal/d from 3y – 5y, B (SE), Linear mixed model:            Data NR, P&gt;0.10</p> <p><b>WC change from 5y – 6y.</b> Per change in kcal/d from 3y – 5y, B (SE), Linear mixed model:            Data NR, P=NS</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, race/ethnicity, anthropometry at baseline</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, SES, physical activity, smoking</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> N/A</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Exposure data based on parental weighed food records</li> <li>• Baseline n NR; No information to assess risk of bias due to missing data</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>            NIH; General Clinical Research Center; Nutrition Center of the Children's Hospital of Philadelphia</p>

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<p><b>Laska, 2012</b><sup>116</sup></p> <p><b>Prospective Cohort Study, Identifying Determinants of Eating and Activity (IDEA) and Etiology of Childhood Obesity (ECHO), United States</b></p> <p>Baseline N=723, Analytic N=535 (Attrition: 26%); Power: NR</p> <p><b>Recruitment:</b> existing cohort, application list from State department of motor vehicles, convenience sample within community, and from membership base of Health Partners (large HMO in Minnesota)</p> <p><b>Participant characteristics: adolescents</b></p> <ul style="list-style-type: none"> <li>Total energy intake: 1982 kcal/d</li> <li>Sex (female): 51%</li> <li>Age: 14.6y</li> <li>Race/ethnicity: ~85% White</li> <li>SES: ~75% Parent college graduate; ~11% Eligible for free/reduced lunch</li> <li>Anthropometrics: BMI 22.0 kg/m<sup>2</sup></li> <li>Physical activity: 310 min/d</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In adolescents, diet soda intake was not significantly associated with changes in BMI or percent body fat at 2y follow-up.</p>	<p><b>Exposure of interest:</b> Diet soda (artificially sweetened soft drinks, fruit drinks, tea, coffee, and/or coffee substitutes)</p> <p><b>Comparator:</b> Diet soda intake (continuous; svg/d)</p> <p>Other exposure measures: SSB</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>Three 24hr recalls (self-report via telephone); represents 2 weekdays and 1 weekend day</li> <li>At baseline, 2y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Males: Diet soda intake at baseline: 0.16 svg/d; 2y follow up: 0.15 svg/d</li> <li>Females: Diet soda intake at baseline: 0.18 svg/d; 2y follow up: 0.25 svg/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 2y follow-up</li> <li>Height measured without shoes using Shorr Height Board to nearest 0.1 cm</li> <li>Weight (to nearest 0.1 kg) and percent body fat (%BF) assessed using digital bioelectrical impedance scale</li> </ul>	<p><b>MALES</b></p> <p><b>BMI</b>, kg/m<sup>2</sup>, Change per svg/d increase of diet soda, Linear regression, <math>\beta</math> (SE)</p> <p>TEI unadj: -0.11 (0.24), P=0.660 TEI adj: -0.09 (0.24), P=0.722</p> <p><b>%BF</b>, Change per svg/d increase of diet soda, Linear regression, <math>\beta</math> (SE)</p> <p>TEI unadj: -0.22 (0.78), P=0.776 TEI adj: 0.09 (0.79), P=0.906</p> <p><b>FEMALES</b></p> <p><b>BMI</b>, kg/m<sup>2</sup>, Change per svg/d increase of diet soda, Linear regression, <math>\beta</math> (SE)</p> <p>TEI unadj: 0.10 (0.23), P=0.683 TEI adj: 0.10 (0.23), P=0.674</p> <p><b>%BF</b>, Change per svg/d increase of diet soda, Linear regression, <math>\beta</math> (SE)</p> <p>TEI unadj: 0.54 (0.35), P=0.122 TEI adj: 0.55 (0.36), P=0.125</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Puberty, study (ECHO vs. IDEA)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 26% without information on non-completers</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b> NCI; NHLBI</p>

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<p><b>Ludwig, 2001</b><sup>146</sup></p> <p><b>Prospective Cohort Study, Planet Health intervention and evaluation project, United States</b></p> <p>Baseline N=780, Analytic N=548 (Attrition overall: 16%); Power: NR</p> <p><b>Recruitment:</b> five randomly assigned control public schools in Massachusetts communities</p> <p><b>Participant characteristics: school-aged children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: 8950 (4500) kJ/d</li> <li>Sex (female): 48%</li> <li>Age: 11.7 (0.8) y</li> <li>Race/ethnicity: 64% White, 15% Hispanic, 14% Afro-American, 8% Asian, 8% American Indian or other</li> <li>SES: Median household income lower than that for all households in MA, USA</li> <li>Anthropometrics: BMI 20.73 (3.99) kg/m<sup>2</sup>; 27% Obese</li> <li>Physical activity: Activity ≥3.5 MET: 1.34 (1.09) hr/d; 38% Exercised to lose weight</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In children, increased diet soda intake was negatively associated with obesity incidence at 19mo follow-up. Baseline diet soda consumption was not related to obesity incidence.</p>	<p><b>Exposure of interest:</b> Diet soda intake</p> <p><b>Comparator:</b> Diet soda intake (continuous; svg/d)</p> <p>Other exposure measures: SSB intake</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Single question on consumption in the past 30 days</li> <li>At baseline, 19mo follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Diet soda intake: NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 19mo follow-up</li> <li>Height measured to nearest 0.1 cm using a Shorr stadiometer</li> <li>Weight measured to nearest 0.1 kg on a portable electronic scale</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>Triceps-skinfold thickness measured twice by trained project staff with calibrated Holtain calipers</li> <li>Obesity defined by a composite indicator of BMI and triceps skinfold thickness ≥85<sup>th</sup>% of age- and sex-specific reference data</li> </ul>	<p><b>BMI</b>, Linear regression, n=548</p> <p><i>Change by diet soda svg/d at baseline:</i></p> <p>Negative <math>\beta</math> (Data NR), P=0.10</p> <p><i>Change by increase in diet soda svg/d:</i></p> <p>Negative <math>\beta</math>, Data NR, P=0.10</p> <p><b>Obesity</b>, Logistic regression, n=398</p> <p><i>Incidence by diet soda svg/d at baseline:</i></p> <p>Data NR, P=0.69</p> <p><i>Incidence by increase in diet soda svg/d:</i></p> <p><b>OR=0.44, P=0.03</b></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b></p> <p>Percent energy from fat, energy-adjusted fruit juice intake, time spent watching television and videos, menarcheal status</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposure measured using single question on frequency not amount</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>NIDDK; NICHD; CDC; Charles H. Hood Foundation</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Macintyre, 2018</b><sup>119</sup>  <b>Prospective Cohort Study, Growing Up in Scotland (GUS), Scotland</b>  Baseline N=3196, Analytic N=2332 (Attrition: 27%); Power: NR</p> <p><b>Recruitment:</b> random sample of aggregated Data Zones, stratified by Local Authority Area and by Scottish Index of Multiple Deprivation</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: NR</li> <li>Sex (female): 49%</li> <li>Age: 4-5y</li> <li>Race/ethnicity: NR</li> <li>SES: Maternal education: 30% Standard grades/intermediate vocational; 33% Higher grades/upper vocational; 28% degree level academic/vocational qualifications</li> <li>Anthropometrics: BMI: 74% Healthy weight; 16% Overweight; 11% Obese</li> <li>Physical activity: 64% Met physical activity guidelines (420 min/wk)</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, consuming ASBs 1-6 times/wk at age 4-5y was significantly associated with greater risk of obesity at 7-8y; however, this did not follow a linear pattern and was only significant for the middle consumption category. There was no association between ASB intake at 4-5y and BMI or risk of overweight at 7-8y.</p>	<p><b>Exposure of interest:</b> Artificially sweetened beverage intake (ASB: diet or low calorie soft drinks, including cans, bottles, mixers, and diet or low-calorie flavored water; not including fresh fruit juice or water)</p> <p><b>Comparators:</b> ASB intake (categorical):</p> <ul style="list-style-type: none"> <li>Never or &lt;1/wk (ref)</li> <li>1-6 times/wk</li> <li>≥1/d</li> </ul> <p>Other exposure measures: SSB</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Parent interview using single question on frequency of intake</li> <li>At Sweep 5: (age 4-5y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>ASB intake: 61%, Never or &lt;1/wk; 14%, 1-6/wk; 25%, ≥1/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At Sweep 4: (age 3-4y), and at ~3y follow-up (Sweep 7: age 7-8y)</li> <li>Height and weight measured on non-carpeted surface by GUS project team following a protocol</li> <li>BMI calculated as kg/m<sup>2</sup></li> <li>BMI classification defined according to British 1990 growth reference curves (Overweight: 85<sup>th</sup>% cutoff, Obesity: 95<sup>th</sup>% cutoff)</li> </ul>	<p><b>Overweight including Obese at 7-8y</b>, Logistic regression, OR (95% CI)  &lt;1/wk (ref) vs  1-6 times/wk: 1.02 (0.71, 1.46), P=0.93  ≥1/d: 0.85 (0.63, 1.15), P=0.28</p> <p><b>Obesity at 7-8y</b>, Logistic regression, OR (95% CI)  &lt;1/wk (ref) vs  <b>1-6 times/wk: 1.57 (1.05, 2.36), P=0.03</b>  ≥1/d: 1.04 (0.74, 1.45), P=0.84</p> <p><b>BMI</b>, kg/m<sup>2</sup>, Linear regression, β (95% CI)  &lt;1/wk (ref) vs  1-6 times/wk: 0.30 (-0.01, 0.61), P=0.06  ≥1/d: -0.11 (-0.32, 0.11), P=0.34</p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: N/A</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, smoking</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Maternal age; mother's BMI; television viewing on weekdays; consumption of breakfast, fruit and vegetables, milk, water, sweets/crisps, and processed meals</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 27% without information on non-completers</li> <li>Exposure data collection tool not validated</li> <li>Exposure data only measured at baseline</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Medical Research Council; Chief Scientist Office of the Scottish Government Directorates</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Marshall, 2018<sup>2</sup></b>  <b>Prospective Cohort Study, Iowa Fluoride and Iowa Bone Development Studies, United States</b>  Baseline N=717 Analytic N=571 (Attrition: 20.4%); Power: NR</p> <p><b>Recruitment:</b> at birth</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: at 2-4.7y, Median~1360 kcal/d</li> <li>Sex (female): 51%</li> <li>Age: Range=2-4.7y</li> <li>Race/ethnicity: Non-Hispanic white 94%</li> <li>SES: Mother had 4y college degree 45%, Household annual income ≥\$60,000 19%</li> <li>Anthropometrics: Weight, Mean~20.0 kg; Height, Mean~111.4 cm</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, when controlling for energy intake, water/other sugar-free beverage intake significantly associated with increases in height.</p>	<p><b>Exposure of interest:</b> Water/other sugar-free beverage intake</p> <p><b>Comparator:</b> Water/other sugar-free beverage intake (continuous; 8 oz/d)</p> <p>Other exposure measures: milk, juice, SSB</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated beverage frequency questionnaire; represents previous week's beverage intakes</li> <li>At 3- to 6-mo intervals: 2-4.7, 5-8.5, 9-10.5, 11-12.5, 13-14.5, and 15-17y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Water/other sugar-free beverage intake at 2-4.7y: Median ~4.7oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At ages 5, 9, 11, 13, 15, 17y</li> <li>Height measured without shoes using stadiometer during clinic visits</li> </ul>	<p><b>Height</b>, cm, <b>Change per 8 oz/d increase</b>; Linear regression:  <b>B: 0.16, 95% CI: 0.01, 0.30, P=0.032</b></p>	<p>TEI adjusted: Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake, protein</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b></p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No information on missing data</li> <li>Registry does not contain data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>  NIH; The Roy J. Carver Charitable Trust; Delta Dental of Iowa Foundation</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Marshall, 2019<sup>41</sup></b>  <b>Prospective Cohort Study, Iowa Fluoride and Iowa Bone Development Studies, United States</b>  Baseline N=720 Analytic N=623 (Attrition: 13.5%); Power: NR</p> <p><b>Recruitment:</b> at birth</p> <p><b>Participant characteristics: children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: at 2-4.7y, Median~1360 kcal/d</li> <li>Sex (female): 51%</li> <li>Age: Range=2-4.7y</li> <li>Race/ethnicity: Non-Hispanic white 94%</li> <li>SES: Mother had 4y college degree 45%; Household annual income ≥\$60,000 19%; Low 25%, Middle 38%, High 38%</li> <li>Anthropometrics: BMI, Mean~16.0 kg/m<sup>2</sup>; BMIZ, Mean~0.31</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In children, when controlling for energy intake, water/other sugar-free beverage intake was significantly associated with increases in BMIZ.</p>	<p><b>Exposure of interest:</b> Water/other sugar-free beverage intake</p> <p><b>Comparator:</b> Water/other sugar-free beverage intake (continuous; 8 oz/d)</p> <p>Other exposure measures: milk, juice, SSB</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated beverage frequency questionnaire; represents previous week's beverage intakes</li> <li>At 3- to 6-mo intervals: 2-4.7, 5-8.5, 9-10.5, 11-12.5, 13-14.5, and 15-17y</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Water/other sugar-free beverage intake at 2-4.7y: Median=4.7 oz/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At ages 5, 9, 11, 13, 15, 17y</li> <li>Height measured without shoes using stadiometer during clinic visits</li> <li>Weight was measured at clinic visit using a standard physician's scale</li> <li>BMIs were calculated from weight and height measures (kg/m<sup>2</sup>)</li> <li>Age- and sex-specific BMI z-scores (BMIZ) calculated 2000 CDC growth charts</li> </ul>	<p><b>BMIZ, Change per 8 oz/d increase in milk, Linear regression:</b>  <b>B: 0.026, 95% CI: 0.006, 0.046, P=0.013</b></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES</li> <li>Other factors considered: total energy intake, protein,</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> other beverage intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>No information on missing data</li> <li>Registry does not contain data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>  NIH; The Roy J. Carver Charitable Trust; Delta Dental of Iowa Foundation</p>

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<p><b>Newby, 2004<sup>43</sup></b>  <b>Prospective Cohort Study, United States</b>            Baseline N=1450, Analytic N=1345 (Attrition: 7%); Power: NR</p> <p><b>Recruitment:</b> WIC clinic, North Dakota</p> <p><b>Participant characteristics: low-income preschool children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean~1747 kcal/d</li> <li>Sex (female): 49.8%</li> <li>Age, Mean (SD): 2.9 (0.7) y</li> <li>Race/ethnicity: White 83%, Native American 11%, Other 6%</li> <li>SES: Maternal education, Mean~12.6y; Poverty level: &lt;100%: 55%; 100-133%: 22%; &gt;133-185%: 23%</li> <li>Anthropometrics: BMI, Mean~16.6 kg/m<sup>2</sup>; At risk of overweight 14%, Overweight 6%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> </ul> <p><b>Summary of findings:</b>            In low-income preschool children, when controlling for energy intake or not, diet soda intake was not significantly associated with changes in weight or BMI</p>	<p><b>Exposure of interest:</b> Diet soda intake (included any no- or low-calorie soda)</p> <p><b>Comparator:</b> Diet soda intake (continuous; oz/d)</p> <p>Other exposure measures: milk, fruit juice, fruit drink, soda</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated FFQ; represents dietary intake during previous month</li> <li>At baseline, 6-12mo follow-up (mean 8.4mo)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Diet soda intake at baseline: Mean~0.7 oz/d; ≥12 oz/d: ~3%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 6-12mo follow-up</li> <li>Height measured by trained staff using wall-mounted measuring board</li> <li>Weight measured by trained staff using standard floor-model beam scale</li> <li>Age- and sex-specific BMI calculated based on 2000 CDC growth charts</li> <li>At risk of overweight (BMI 85<sup>th</sup> to &lt;95<sup>th</sup>%); Overweight (BMI≥95<sup>th</sup>%)</li> </ul>	<p><b>Weight</b>, Linear regression  <b>Change per oz/d increase, <math>\beta</math> (SE):</b>            TEI adj: 0.01 (0.02), P=0.92</p> <p><b>BMI</b>, Linear regression  <b>Change per oz/d increase, <math>\beta</math> (SE):</b>            TEI adj: 0.01 (0.02), P=0.83</p> <p>Estimates remained similar when TEI was omitted from model. (Data NR)</p>	<p><b>TEI adjusted:</b> Yes and No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> birth weight, other beverages</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Potential selection bias by only including participants with 2 WIC clinic visits 6-12 months apart</li> <li>No preregistered data analysis plan</li> <li>Racial/ethnic minorities under-represented in study sample</li> </ul> <p><b>Funding sources:</b>            USDA; NIH Health Harvard Education Program in Cancer Prevention Control; Boston Obesity Nutrition Research Center</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Striegel-Moore, 2006<sup>55*</sup></b>  <b>Prospective Cohort Study, NHLBI Growth and Health Study, United States</b></p> <p>Baseline N=2379 Analytic N=2371 (Attrition: 0.3%); Power: n=1150 per group at 90% power to detect compare change in subscapular skinfold between Black and White girls</p> <p><b>Recruitment:</b> public and parochial schools, local health maintenance organization and Girl Scout troops</p> <p><b>Participant characteristics: adolescent girls</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 100%</li> <li>• Age: Mean ~10y</li> <li>• Race/ethnicity: Black 51%, White 49%</li> <li>• SES: &lt;\$10K: 17%; \$10&lt;20K: 14%; \$20&lt;30K: 15%; \$30&lt;40K: 14%; \$40&lt;50K: 12%; \$50&lt;75K: 17%; ≥\$75K: 6%</li> <li>• Anthropometrics: Weight: ~ 37kg; Height: ~141 cm</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b></p> <p>In adolescent girls, diet soda intake was not significantly associated with changes in BMI at 10y follow-up.</p> <p>* Some info on baseline data and methodology from: Obesity and CVD risk factors in black and white girls: the NHLBI Growth and Health Study. Am J Public Health. 1992; 82:1613-1620.</p>	<p><b>Exposure of interest:</b> Diet soda intake (artificially sweetened carbonated soft drinks, diet or low calorie)</p> <p><b>Comparator:</b> Diet soda intake (continuous; 100 g/d)</p> <p>Other exposure measures: milk, regular soda, fruit juice, fruit drinks, coffee/tea</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated 3-d food records; represents usual intake over 3 consecutive days (2 weekdays and 1 weekend day)</li> <li>• At baseline, and annually for years 1-5, then at years 7, 8, 10</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Diet soda intake, g/d, Mean (SE): White, 22.36 (4.52); Black, 7.20 (1.75)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• Baseline, annually until 10y follow-up</li> <li>• Weight measured twice by research staff using electronic scale</li> <li>• Height measured twice by research staff using stadiometer</li> <li>• BMI calculated as weight in kilograms divided by height in meters squared</li> </ul>	<p><b>BMI</b>, Linear regression  <b>Change per 100g/d increase:</b>  B: -0.010, SE: 0.013, P&gt;0.05</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  consumption of other beverage types, site</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Missing data not clearly reported</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NHLBI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Zheng, 2015<sup>1</sup></b>  <b>Prospective Cohort Study, Childhood Asthma Prevention Study, Australia</b>  Baseline N=237 Analytic N=158 (Attrition: 33.3%); Power: NR</p> <p><b>Recruitment:</b> pregnant women from antenatal clinics</p> <p><b>Participant characteristics: 8yo children</b></p> <ul style="list-style-type: none"> <li>Total energy intake: Mean ~8.0 MJ/d</li> <li>Sex (female): 48%</li> <li>Age: Mean ~8.0y</li> <li>Race/ethnicity: Mother born in Australia/New Zealand ~78%; Father born in Australia/New Zealand ~73%</li> <li>SES: Maternal education level &gt;12y ~55%; Paternal education level &gt;12y ~58%; Living in disadvantaged area ~20%</li> <li>Anthropometrics: BMI z-score, Mean (SD): 0.4(1.0); Overweight/obese 27.2%</li> <li>Physical activity: NR</li> <li>Smoking: NR</li> <li>Intervention group: 54.9%</li> </ul> <p><b>Summary of findings:</b>  In children, diet drink consumption was associated with decreases in BMIZ and %BF when TEI was adjusted for; when TEI was not adjusted for this association was only significant for BMIZ. Using a substitution model, substituting SSBs with diet drinks was associated with decreased BMIZ and %BF; however, this was no longer significant when the model adjusted for beverage energy.</p>	<p><b>Exposure of interest:</b> Diet drink intake (low energy drinks sweetened with artificial sweeteners)</p> <p><b>Comparator:</b> Diet drink intake (100 g/d) modeled continuously</p> <p>Other exposure measures: milk, water, SSB, 100% fruit juice, and liquid energy (energy from all beverages)</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Three 24-hr dietary recalls via phone using multiple pass approach completed by children with parental assistance; Represents usual dietary intake on nonconsecutive weekdays and weekends</li> <li>At 1y follow-up (age 9y)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Diet drink intake at baseline (g/d), Mean (SD): ~90(89)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>Baseline (age 8y), and 3.5y follow-up (age 11.5y)</li> <li>Weight measured to nearest 0.1kg</li> <li>Height measured using stadiometer</li> <li>Age- and sex-specific BMI z-scores (BMIZ) calculated using 2000 CDC growth charts</li> <li>Percentage body fat (%BF) measured by bioimpedance analysis</li> </ul>	<p><b>Change per 100 g/d increase, Linear regression, <math>\beta</math> (SE):</b>  <b>BMIZ:</b>  TEI unadj: -0.18 (0.007), P=0.02  TEI adj: -0.20 (0.07), P=0.01</p> <p><b>%BF:</b>  TEI unadj: -1.23 (0.70), P=0.09  TEI adj: -1.41 (0.70), P=0.046</p> <p><b>Change per 100 g/d substitution of SSB, Linear regression, <math>\beta</math> (SE):</b>  <b>BMIZ:</b>  Bev EI unadj: -0.28 (0.08), P=0.001  Bev EI adj: -0.28 (0.10), P=0.16</p> <p><b>%BF:</b>  Bev EI unadj: -2.86 (0.92), P=0.002  Bev EI adj: -2.90 (1.14), P=0.12</p>	<p><b>TEI adjusted:</b> Yes and no</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: physical activity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> Maternal age at birth, presence of gestational diabetes, exclusive breastfeeding at 3mo, pubertal status, randomization group (omega-3 fatty acid dietary supplementation and house dust mite reduction); Substitution model: EI from non-bev sources</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Anthropometric measures not taken at same time as dietary data</li> <li>Exposure data collected at 1 time to represent 3.5y period</li> </ul> <p><b>Funding sources:</b>  National Health and Medical Research Council of Australia; Cooperative Research Centre for Asthma; New South Wales Department of Health; Children's Hospital Westmead</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Zheng, 2015<sup>62</sup></b>  <b>Prospective Cohort Study, Healthy Start Study (RCT), Denmark</b>  Baseline N=552 Analytic N=352 (Attrition: 36.2%); Power: NR  <b>Recruitment:</b> Danish National Birth Register</p> <p><b>Participant characteristics: normal weight children at high-risk of overweight</b></p> <ul style="list-style-type: none"> <li>Total energy intake, MJ/d, Mean (SD): 4.97 (0.95)</li> <li>Sex (female): 45.2%</li> <li>Age: 4.1 (1.1) y</li> <li>Race/ethnicity: NR</li> <li>SES: Maternal education level, Tertiary or above: 78.0%; Paternal education level, Tertiary or above: 61.0%; Parents divorced 5.6%</li> <li>Anthropometrics: Mean (SD), Body weight (kg): 18.0 (3.3); BMI z-score: 0.3 (0.9)</li> <li>Physical activity: High 59.2%</li> <li>Smoking: NR</li> <li>Intervention group: 46.0%</li> </ul> <p><b>Summary of findings:</b>  In children, when controlling for energy intake, increasing diet drink intake was not significantly associated with changes in BMIZ or body weight. Substitution of sugary drinks with diet drinks was associated with increased BMIZ, but not associated with changes in body weight.</p>	<p><b>Exposure of interest:</b> Diet drink intake (artificially-sweetened beverages)</p> <p><b>Comparator:</b> Diet drink intake (100 g/d) modeled continuously</p> <p>Other exposure measures: milk, water, sugary drinks</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>4-d dietary record completed by parents; represents dietary intake on both weekdays and weekends</li> <li>At baseline, 1.5y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Diet drink intake at baseline (g/d), Mean (SD): 24.8 (65.0)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 1.5y follow-up</li> <li>Height measured using stature meter</li> <li>Weight measured using mechanical weight or beam-scale</li> <li>Age- and sex-specific BMI z-scores (BMIZ) calculated using Lambda-Mu-Sigma method</li> </ul>	<p><i>Nutrient Residual Model</i> (includes beverage intake residuals and total energy intake)  <b>BMIZ</b>, Linear regression  <b>Change per 100 g/d increase:</b>  B: -0.09, SE: 0.07, P=0.15  <b>Body weight</b>, Linear regression  <b>Change per 100 g/d increase:</b>  B: -0.09, SE: 0.15, P=0.53</p> <p><i>Energy Partition Model</i> (includes absolute amount of individual beverage intake and energy from non-beverage sources)  <b>BMIZ</b>, Linear regression  <b>Change per 100 g/d increase:</b>  B: -0.10, SE: 0.07, P=0.14  <b>Body weight</b>, Linear regression  <b>Change per 100 g/d increase:</b>  B: -0.10, SE: 0.15, P=0.48</p> <p><i>Substitution Model</i> (includes absolute intakes of total beverages and individual beverage alternative for sugary drinks)  <b>BMIZ</b>, Linear regression  <b>Change per 100 g/d substitution of sugary drinks:</b>  <b>B: 0.07, SE: 0.08, P=0.04</b>  <b>Body weight</b>, Linear regression  <b>Change per 100 g/d substitution of sugary drinks:</b>  B: 0.02, SE: 0.18, P=0.89</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, SES, anthropometry at baseline, physical activity</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, smoking</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  intervention allocation, parents divorced, number of siblings living with the child, maternal pre-pregnancy overweight</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Attrition 36% without information on non-completers</li> <li>No preregister analysis plan</li> </ul> <p><b>Funding sources:</b>  None</p>

**Table 28. Risk of bias for prospective cohort studies examining LNCSB consumption and growth, size, body composition and risk of overweight and obesity in children<sup>lix, lx</sup>**

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Berkey, 2004 <sup>7</sup>	Serious	Low	Low	Low	Moderate	Moderate	Serious
Blum, 2005 <sup>11</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Davis, 2018 <sup>143</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Dong, 2015 <sup>15</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Field, 2014 <sup>103</sup>	Serious	Low	Low	Low	Moderate	Serious	Moderate
Haines, 2007 <sup>26</sup>	Serious	Low	Low	Low	Moderate	Moderate	Moderate
Hasnain, 2014 <sup>27</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Kral, 2008 <sup>33</sup>	Serious	Low	Moderate	Low	No information	Low	Moderate
Laska, 2012 <sup>116</sup>	Moderate	Low	Low	Low	Moderate	Low	Moderate
Ludwig, 2001 <sup>146</sup>	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Macintyre, 2018 <sup>119</sup>	Serious	Low	Serious	Moderate	Moderate	Low	Moderate
Marshall, 2018 <sup>2</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Marshall, 2019 <sup>41</sup>	Serious	Low	Low	Low	Moderate	Low	Moderate
Newby, 2004 <sup>43</sup>	Serious	Moderate	Low	Low	Low	Low	Moderate
Striegel-Moore, 2006 <sup>55</sup>	Serious	Low	Low	Low	No information	Low	Moderate
Zheng, 2015 <sup>1</sup>	Serious	Low	Moderate	Low	Low	Low	Moderate
Zheng, 2015 <sup>62</sup>	Serious	Low	Serious	Moderate	Serious	Low	Moderate

<sup>lix</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>lx</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

**Table 29: Summary of articles examining the relationship between LNCSB consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>lxi</sup>**

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
CONTROLLED TRIALS			

<sup>lxi</sup> Abbreviations: BMI: body mass index; CI: confidence interval; CTSA: Clinical and Translational Science Awards; d: day(s); DB: diet beverage; DM: diabetes militis; DXA or DEXA: dual-energy X-ray absorptiometry; FFQ: food frequency questionnaire; HISB: high-intensity sweetened beverage; HR: hazard ratio; LNCSB: low and no calorie sweetened beverages; NA: not applicable; NCI: National Cancer Institute; NCRR: National Center for Research Resources; NHLBI: National Heart, Lung, and Blood Institute; NIA: National Institute on Aging; NICHD: National Institute of Child Health and Human Development; NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases; NIH: National Institutes of Health; NNS: non-nutritive sweeteners; NR: not reported; NS: not significant; OR: odds ratio; RCT: randomized controlled trial; RR: relative risk; SD: standard deviation; SE: standard error; SEM: standard error of the mean; SES: socioeconomic status; SSB: sugar-sweetened beverage; TEI: total energy intake; UB: unsweetened beverage; WC: waist circumference; wk: week(s); y: year(s)  
 Red font indicates a statistically significant detrimental relationship, and green font indicates a statistically significant beneficial relationship.



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Bonnet, 2018<sup>142</sup></b>  <b>Crossover RCT, ‘Comparison of the Effects of a 12-Week Consumption of Two Carbonated Beverages on Insulin Sensitivity’ (SEDULC), France</b></p> <p>Baseline N=60, Analytic N=50; Attrition: 17%; Power: to demonstrate non-inferiority between 2 beverages for main outcome (insulin sensitivity) with a type I error of 5% and a type II error of 20%, an estimated minimum of 22 individuals were needed for the analysis</p> <p><b>Recruitment:</b> public advertisements in newspapers and local database of volunteers for clinical trials</p> <p><b>Participant characteristics: non-overweight or overweight adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~2645 kcal/d</li> <li>• Sex (female): 56%</li> <li>• Age: 31.1 (10.3) y</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI 24.7 (3.2) kg/m<sup>2</sup>; WC 82.6 (8.6) cm</li> <li>• Physical activity: NR</li> <li>• Smoking: NR</li> </ul> <p><b>Summary of findings:</b>  In adults, drinking a high-intensity sweetener beverage containing aspartame and acesulfame K (660 mL/d) compared to an unsweetened beverage (660 mL/d) for 12wk did not result differences in weight, BMI, or waist circumference. There was no difference in energy intake in the 12 weeks when the high-intensity sweetened beverage was consumed compared to when the unsweetened beverage was consumed.</p>	<p><b>Intervention:</b> High-intensity sweetener beverage (HISB): carbonated water containing aspartame and acesulfame K (2 cans of 330 mL/d), n=50</p> <p><b>Comparator:</b> Unsweetened beverage (UB): carbonated water (2 cans of 330 mL/d), n=50</p> <p>Other interventions: N/A</p> <p><u>Intervention duration:</u> 12wk each arm, with 4wk washout period between arms (12wk+4wk wash-out +12wk=28wk)</p> <p><u>Intervention compliance:</u> NR</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Habitual intake of HISB: &lt;1 can (inclusion criteria)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 12wk follow-up (start and end of each study arm)</li> <li>• Weight and waist size were measured at assessment visit (methods NR)</li> </ul>	<p><b>Weight</b>, kg, Mean (SEM)  <b>Change over time, within group:</b> 0wk, 12wk  UB: 73.99 (1.4), 74.02 (0.4)  HISB: 74.65 (1.4), 73.43 (0.4)  <b>Change over 12wk between groups:</b>  UB: 0.34 (0.4)  HISB: -0.25 (0.4)  P=0.26</p> <p><b>BMI</b>, kg/m<sup>2</sup>, Mean (SEM)  <b>Change over time, within group:</b> 0wk, 12wk “BMI remained stable over each intervention period without differences between the periods”, Data NR, P=NS  <b>Change over 12wk between groups:</b>  Data NR, P=NS</p> <p><b>Waist circumference</b>, cm, Mean (SEM)  <b>Change over time, within group:</b> 0wk, 12wk  UB: 82.45 (1.1), 82.70 (0.6)  HISB: 82.47 (1.1), 82.90 (0.7)  <b>Change over 12wk between groups:</b>  UB: 0.76 (0.6)  HISB: 0.96 (0.7)  P=0.84</p>	<p><b>TEI adjusted:</b> No (NS between intervention arms)</p> <p><b>Energy Intake, kcal/d, Mean (SEM)</b>  <b>Change within group:</b> 0wk, 12wk  UB: 2560 (124), 2573 (81)  HISB: 2615 (124), 2500 (81)  <b>Change over 12wk between groups:</b>  UB: 46.6 (81)  HISB: -119 (81)  P=0.42</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: anthropometry at baseline</li> <li>• Other factors considered: total energy intake, protein, alcohol (all NS at baseline)</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, physical activity, smoking</li> <li>• Other factors considered: timing, temporal use, sugar, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Sequence</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Randomization and allocation methods NR</li> <li>• Compliance measures NR</li> <li>• Power not based on these outcomes (may be underpowered)</li> <li>• Trial registry did not include data analysis plan; registry does not contain these outcomes as 1° or 2° outcomes</li> </ul> <p><b>Funding Sources:</b>  Institute for European Expertise in Physiology (Paris, France); The Coca-Cola Company (USA)</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Madjid, 2015</b><sup>147</sup> (see <b>Madjid, 2018</b><sup>148</sup>)  <b>RCT, Iran</b>  Baseline N=71, Analytic N=62; Attrition: 13%; Power: final sample size of 56 for diff 2.0±2.5 kg in weight loss, <math>\alpha=0.05</math>, <math>\beta=85\%</math></p> <p><b>Recruitment:</b> participants attending NovinDiet Clinic weight-loss clinic</p> <p><b>Participant characteristics: overweight and obese women, habitual consumers of diet beverages</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~2447 kcal/d</li> <li>• Sex (female): 100%</li> <li>• Age: ~32y</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI ~33.7 kg/m<sup>2</sup></li> <li>• Physical activity: NR</li> <li>• Smoking: 100% nonsmokers</li> </ul> <p><b>Summary of findings:</b>  In overweight and obese women participating in a 24 wk weight loss program, drinking diet beverages (250 mL/d) after lunch compared to water (250 mL/d) resulted in lower decreases in weight and BMI after 24wk. There was no difference between groups in waist circumference. Daily energy intake was greater at the end of the intervention in the group that drank diet beverages daily compared to water.</p>	<p><b>Intervention (DB):</b> Diet beverage, 1/d, 250 mL after lunch, 5d/wk; drink water remainder of week; provided with beverages; n=32/36</p> <p><b>Comparator (Water):</b> replaced regular consumption of diet bevs with water; drank 250 mL water after lunch; n=30/35</p> <p><b>All participants:</b> Phase 1 (24wk): weight loss phase: started a hypoenergetic diet (500-1000kcal deficit based on EER) according to NovinDiet protocol, which included advice to gradually increase activity levels to achieve 60 min of moderate activity 5d/wk; Phase 2 (53wk): weight maintenance phase: monthly group and individual sessions with dietitian</p> <p><u>Intervention duration:</u> 24wk</p> <p><u>Intervention compliance:</u> NR</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Habitual consumers of DB (inclusion criteria)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 12wk and 24wk follow-up</li> <li>• Weight measured by a dietitian using a digital calibrated scale</li> <li>• Height measured by a dietitian using a wall-mounted stadiometer</li> <li>• BMI calculated as kg/m<sup>2</sup></li> <li>• Waist circumference (WC) measured by dietitian with a rigid measuring tape at smallest horizontal circumference between ribs and iliac crest</li> </ul>	<p><b>Weight</b>, kg, Mean (SD)  <b>Change within group:</b> 0wk, 24wk  Water: 88.7 (8.9), 79.9 (8.3), <b>P&lt;0.001</b>  DB: 87.9 (9.9), 80.3 (10.2), <b>P&lt;0.001</b>  <b>Change over time, between groups:</b>  <b>Water: -8.8 (1.9)</b>  <b>DB: -7.6 (2.1)</b>  <b>Group*time, P=0.015</b></p> <p><b>BMI</b>, kg/m<sup>2</sup>, Mean (SD)  <b>Change within group:</b> 0wk, 24wk  Water: 33.9 (3), 30.6 (2.8), <b>P&lt;0.001</b>  DB: 33.5 (3.6), 30.6 (3.8), <b>P&lt;0.001</b>  <b>Change over time, between groups:</b>  <b>Water: -3.4 (0.7)</b>  <b>DB: -2.9 (0.8)</b>  <b>Group*time, P=0.002</b></p> <p><b>WC</b>, cm, Mean (SD)  <b>Change within group:</b> 0wk, 24wk  Water: 104.9 (5.9), 96.3 (5.7), <b>P&lt;0.001</b>  DB: 103.7 (6.2), 95.8 (6.7), <b>P&lt;0.001</b>  <b>Change over time, between groups:</b>  Water: -8.6 (3.4)  DB: -7.9 (2.7)  Group*time, P=0.354</p>	<p><b>TEI adjusted:</b> No (NS at baseline)</p> <p><b>Energy Intake, kcal/d, Mean (SD)</b>  <b>Change within group:</b> 0wk, 24wk  Water: 2457 (303), 1871 (203), <b>P&lt;0.001</b>  DB: 2438 (295), 1984 (348), <b>P&lt;0.001</b>  <b>Group*time, P=0.015</b></p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, smoking</li> <li>• Other factors considered: total energy intake, protein, fiber, medications</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES, physical activity</li> <li>• Other factors considered: timing, temporal use, sugar, energy density, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  NS at baseline: fat intake, carbohydrate intake, marital status, cholesterol (total, HDL, LDL), triglycerides, fasting plasma glucose, HbA1c, insulin, HOMA-IR</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No measure of compliance</li> <li>• Trial registry did not include data analysis plan</li> </ul> <p><b>Funding Source:</b>  School of Life Sciences, University of Nottingham, United Kingdom; Digestive Disease Research Institute affiliated with Tehran University of Medical Sciences</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Madjid, 2018</b><sup>148</sup> (see <b>Madjid, 2015</b><sup>147</sup>) <b>RCT, Iran</b></p> <p>Baseline N=71, Analytic N=56; Attrition: 21% (ITT analysis conducted); Power: With the assumption of a detectable difference in weight loss of 2.5 kg at 18 months and an SD= 3 kg, 51 participants were required to achieve 85% power of detecting a treatment effect (two-sided significance level of 5%)</p> <p><b>Recruitment:</b> participants attending NovinDiet Clinic weight-loss clinic</p> <p><b>Participant characteristics: overweight and obese women</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~2447 kcal/d</li> <li>• Sex (female): 100%</li> <li>• Age: ~32y</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI ~33.7 kg/m<sup>2</sup></li> <li>• Physical activity: NR</li> <li>• Smoking: 100% nonsmokers</li> </ul> <p><b>Summary of findings:</b></p> <p>In overweight and obese women participating in a 24wk weight loss and 53wk weight maintenance program, drinking diet beverages (250 mL/d) after lunch compared to water (250 mL/d) resulted in lower decreases in weight and BMI after 12 and 18mo. There was no change in waist circumference. Energy intake was greater after the intervention in the group that drank diet beverages daily compared to water.</p>	<p><b>Intervention (DB):</b> Diet beverage, 1/d, 250 mL after lunch, 5d/wk; drink water remainder of week; provided with beverages; n=29/36</p> <p><b>Comparator (Water):</b> replaced regular consumption of diet bevs with water; drank 250 mL water after lunch; n=27/35</p> <p><b>All participants:</b> started a hypoenergetic diet (500-1000kcal deficit based on EER) according to NovinDiet protocol, which included advice to gradually increase activity levels to achieve 60 min of moderate activity 5d/wk</p> <p><u>Intervention duration:</u> 24wk</p> <p><u>Intervention compliance:</u> NR</p> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Habitual consumers of DB (inclusion criteria)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, 24wk and 77wk follow-up</li> <li>• Weight measured by a dietitian using a digital calibrated scale</li> <li>• Height measured by a dietitian using a wall-mounted stadiometer</li> <li>• BMI calculated as kg/m<sup>2</sup></li> <li>• Waist circumference (WC) measured by dietitian with a rigid measuring tape at smallest horizontal circumference between ribs and iliac crest</li> </ul>	<p><b>Weight</b>, kg, Mean (SD) <b>Change within group:</b> 0wk, 24wk, 77wk Water: 88.2 (8.8), 79.7 (7.9), 78 (6.1), P=NS DB: 87.6 (9.8), 80 (9.7), 79.8 (8.2), P=NS <b>Change over 12mo, between groups:</b> <b>Water: -1.7 (2.8)</b> <b>DB: -0.1 (2.7)</b> <b>P=0.001</b> <b>Change over 18mo, between groups:</b> <b>Group*time, P=0.005</b></p> <p><b>BMI</b>, kg/m<sup>2</sup>, Mean (SD) <b>Change within group:</b> 0wk, 24wk, 77wk Water: 33.9 (3), 30.6 (2.7), 30 (2.3), P=NS DB: 33.5 (3.6), 30.6 (3.5), 30.5 (2.9), P=NS <b>Change over 12mo, between groups:</b> <b>Water: -0.7 (1.0)</b> <b>DB: -0.05 (1.1)</b> <b>P=0.003</b> <b>Change over 18mo, between groups:</b> <b>Group*time, P=0.005</b></p> <p><b>WC</b>, cm, Mean (SD) <b>Change within group:</b> 24wk, 77wk Water: 106 (5.8), 96 (5.6), 94.3 (3.9), <b>P&lt;0.001</b> DB: 103.5 (5.9), 95.8 (6.7), 94.5 (4.7), <b>P&lt;0.001</b> <b>Change over 12mo, between groups:</b> Water: -2.1 (3.1) DB: -1.2 (3.2) P=0.188 <b>Change over 18mo, between groups:</b> Group*time, P=0.286</p>	<p><b>TEI adjusted:</b> No (NS at baseline)</p> <p><b>Energy Intake, kcal/d, Mean (SD)</b> <b>Change within group:</b> 0wk, 77wk Water: 2461 (300), 1761 (124), <b>P&lt;0.001</b> DB: 2429 (300), 1935 (224), <b>P&lt;0.001</b> <b>Change over 18mo, between groups:</b> <b>P=0.001</b></p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, smoking</li> <li>• Other factors considered: total energy intake, protein, fiber, medications</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES, physical activity</li> <li>• Other factors considered: timing, temporal use, sugar, energy density, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b> NS at baseline: fat intake, marital status, cholesterol (total, HDL, LDL), triglycerides, fasting plasma glucose, HbA1c, insulin, HOMA-IR</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No measure of compliance</li> <li>• Trial registry did not include data analysis plan</li> </ul> <p><b>Funding Source:</b> Digestive Disease Research Institute affiliated with Tehran University of Medical Sciences</p>

**Peters, 2016**<sup>150</sup> (see **Peters, 2014**<sup>151</sup>)

#### **RCT, United States**

Baseline N=303, Analytic N=222;  
Attrition: 27%; Power: Assuming the true difference was 0.73 kg (1/3 of the equivalence margin) and common SD of 4.2 kg, a sample size of 63 per arm was required using two, one-sided t-tests to ensure at least 80% power with an alpha level of  $P < 0.05$  to establish equivalence

**Recruitment:** from the general population through the use of flyers, e-mails, and other advertisements (e.g., radio)

#### **Participant characteristics: overweight and obese adults**

- Total energy intake: NR
- Sex (female): ~82%
- Age: ~48y
- Race/ethnicity: ~62% White, ~28% black/African American
- SES: NR
- Anthropometrics: ~94kg; BMI ~33.5
- Physical activity: NR
- Smoking: NR

#### **Summary of findings:**

After a 1yr weight loss intervention in overweight and obese adults, those who drank  $\geq 24$  fl oz/d of non-nutritive sweetened beverages lost more weight and had greater reductions in waist circumference compared to those who drank  $\geq 24$  fl oz/d of water. A greater percentage of participants who drank NNS achieved 5% weight loss after 1y compared to those who drank water.

**Intervention (NNS group, n=158):** asked to consume  $\geq 24$  fl oz/d (710 ml) of NNS beverages for 1y, with unrestricted water consumption. Premixed beverages containing NNS and  $< 5$  kcal/8-oz serving (237 ml) qualified as NNS beverages

**Comparator (Water group, n=150):** asked to consume  $\geq 24$  fl oz/d (710 ml) of water for 1y and refrain from NNS beverage consumption. Instructed to not add NNS (e.g., aspartame, sucralose, stevia, diet creamers) to beverages such as coffee/tea; permitted to consume foods containing NNS, although not instructed to do so as part of weight loss program

**All participants:** 12wk weight loss phase: weekly, 60-min instructional classes from comprehensive cognitive-behavioral weight loss intervention (The Colorado Weigh); 40wk weight maintenance phase: 9 monthly group meetings, weighed monthly, advised to consume 25-35% of calories from fat and include 6d/wk of unsupervised exercise to meet weight loss maintenance recommendation of 60 min of moderate activity daily; Participants were given 4 manufacturer coupons redeemable for a monthly supply of NNS beverages or bottled water

Intervention duration: 1y (first 12 wk weight loss; next 40 wk weight maintenance)

Intervention compliance: Participants were asked to record their daily beverage intake using paper logs; compliance was high

#### **Study beverage intake:**

- Inclusion criteria: drink NSS bevs 3/wk

#### **Outcome assessment methods/timing:**

- At baseline, 12wk, 52 wk
- Height measured with stadiometer
- Weight measured on a digital scale
- Waist circumference (WC) measured at top of iliac crest, based on 2 consecutive measures

**Weight loss at 1yr,** kg, Mean (SD)

**Over time, within group:** Baseline, 52 wk

**Water: 93.15 (12.94); 90.70 (13.70),  $P < 0.001$**

**NNS: 93.91 (13.46); 87.70 (14.79),  $P < 0.001$**

**Change between groups:  $P < 0.001$**

#### **% Achieved 5% weight loss**

**Water (n=149): 25.5%**

**NSS (n=154): 44.2%,  $P < 0.001$**

**WC at 1yr,** cm, Mean (SD)

**Over time, within group:** Baseline, 52 wk

**Water: 107.10 (0.91), 102.93 (1.00),  $P < 0.001$**

**NNS: 108.00 (0.89), 99.33 (0.97),  $P < 0.001$**

**Change between groups:  $P < 0.001$**

**TEI adjusted:** No

#### **Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, anthropometry at baseline
- Other factors considered: medications

#### **Confounders NOT accounted for:**

- Key confounders: SES, physical activity, smoking
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, supplements, alcohol

**Additional model adjustments:** N/A

#### **Limitations:**

- Allocation concealment NR
- 27% attrition with no info on non-completers

#### **Funding Source:**

American Beverage Association

**Peters, 2014<sup>151</sup>** (see **Peters, 2016<sup>150</sup>**)

#### **RCT, United States**

Baseline N=303, Analytic N=222;  
Attrition: 27%; Power: Assuming the true difference was 0.73 kg (1/3 of the equivalence margin) and common SD of 4.2 kg, a sample size of 63 per arm was required using two, one-sided t-tests to ensure at least 80% power with an alpha level of  $P < 0.05$  to establish equivalence

**Recruitment:** from the general population through the use of flyers, e-mails, and other advertisements (e.g., radio)

#### **Participant characteristics: overweight and obese adults**

- Total energy intake: NR
- Sex (female): ~82%
- Age: ~48y
- Race/ethnicity: ~62% White, ~28% black/African American
- SES: NR
- Anthropometrics: ~94kg; BMI ~33.5
- Physical activity: NR
- Smoking: NR

#### **Summary of findings:**

After a 12 week weight loss intervention in overweight and obese adults, those who drank  $\geq 24$  fl oz/d of non-nutritive sweetened beverages lost more weight compared to those who drank  $\geq 24$  fl oz/d of water. A greater percentage of participants who drank NNS achieved 5% weight loss after 12 weeks compared to those who drank water.

**Intervention (NNS group, n=158):** asked to consume  $\geq 24$  fl oz/d (710 ml) of NNS beverages for 1y, with unrestricted water consumption. Premixed beverages containing NNS and  $< 5$  kcal/8-oz serving (237 ml) qualified as NNS beverages

**Comparator (Water group, n=150):** asked to consume  $\geq 24$  fl oz/d (710 ml) of water for 1y and refrain from NNS beverage consumption. Instructed to not add NNS (e.g., aspartame, sucralose, stevia, diet creamers) to beverages such as coffee/tea; permitted to consume foods containing NNS, although not instructed to do so as part of weight loss program

**All participants:** 12wk weight loss phase: weekly, 60-min instructional classes from comprehensive cognitive-behavioral weight loss intervention (The Colorado Weigh); 40wk weight maintenance phase: 9 monthly group meetings, weighed monthly, advised to consume 25-35% of calories from fat and include 6d/wk of unsupervised exercise to meet weight loss maintenance recommendation of 60 min of moderate activity daily; Participants were given 4 manufacturer coupons redeemable for a monthly supply of NNS beverages or bottled water

Intervention duration: 1y (first 12 wk weight loss; next 40 wk weight maintenance)

Intervention compliance: Participants were asked to record their daily beverage intake using paper logs; compliance was high

#### **Study beverage intake:**

- Inclusion criteria: drink NSS bevs 3/wk

#### **Outcome assessment methods/timing:**

- At baseline, 12wk
- Height measured with stadiometer
- Weight measured on a digital scale

Waist circumference (WC) measured at top of iliac crest, based on 2 consecutive measures

Weight loss at 12wk, kg, Mean (SD)  
**Over time, within group:** Baseline, 12 wk

**Water: 93.15 (12.94); 89.06 (12.86),  $P < 0.0001$**

**NNS: 93.91 (13.46); 87.97 (13.39),  $P < 0.0001$**

**Change between groups:  $P < 0.0001$**

#### % Achieved 5% weight loss

**Water (n=149): 43.0%**

**NSS (n=154): 64.3%,  $P = 0.0002$**

WC at 12wk, cm, Mean (SD)

**Over time, within group:** Baseline, 12 wk

**Water: 107.10 (0.87), 102.74 (0.90),  $P < 0.0001$**

**NNS: 108.00 (0.86), 102.27 (0.88),  $P < 0.0001$**

**Change between groups:  $P = 0.0528$**

**TEI adjusted:** No

#### **Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, anthropometry at baseline
- Other factors considered: medications

#### **Confounders NOT accounted for:**

- Key confounders: SES, physical activity, smoking
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, supplements, alcohol

**Additional model adjustments:** N/A

#### **Limitations:**

- Allocation concealment NR
- 27% attrition with no info on non-completers

#### **Funding Source:**

American Beverage Association



**Vazquez-Duran, 2016**<sup>137</sup>

**RCT, Clinical Trial, Mexico**

Baseline N=148, Analytic N=146 (Attrition: 1%); Power: a sample size of 31, which was increased by 20% loss to follow up, gave a total of 37 patients in each group.  $\alpha=0.05$ ,  $\beta=80\%$  to detect -1.6% change in BMI in intervention group with SD 0.8

**Recruitment:** María Elena Maza Brito  
School of Nursing in Mexico City

**Participant characteristics: young adults consuming  $\geq 12$  oz/d SSB**

- Total energy intake: NR
- Sex (female): 81%
- Age: 21.99 (0.25) y
- Race/ethnicity: NR
- SES: all nursing students
- Anthropometrics: BMI: 26.24 (0.36) kg/m<sup>2</sup>; Overweight: 45%; Obesity: 16%
- Physical activity: <1hr/d of vigorous physical activity (inclusion criteria)
- Smoking: NR

**Summary of findings:**

In young adults, drinking beverages with non-caloric sweeteners for 6 mo compared to participants who were not permitted sweetened beverages for 6 mo resulted in lower decreases in BMI, waist circumference, and resistance/height (a measure of body composition). There was no difference between groups for hip circumference or phase angle (also a measure of body composition).

**Intervention:**

Only beverages with non-caloric sweeteners allowed (including plain water, lemon and hibiscus flavored water, coffee and tea without sugar), n=50

**Comparator:** No sweetened beverages permitted (only plain water, lemon and hibiscus flavored water, coffee and tea without sugar), n=49

Other interventions: Usual intake, n=49

Intervention duration: 6mo

Intervention compliance: 24hr food record 1x/week for full 6-month intervention

**Study beverage intake:**

- Habitual SSB intake:  $\geq 12$  oz/d

**Outcome assessment methods/timing:**

- At baseline, 3mo and 6mo follow-up
- Weight and height measured according to anthropometric standardization reference manual
- Body composition (resistance/height and phase angle) evaluated by bioelectric impedance analysis
- Waist, hip, and arm circumferences evaluated according to the anthropometric reference manual

All Linear regression, Mean (SD)

**BMI % of change**

**Change over time, within group:** 3mo, 6mo

ASB: -0.61 (0.08), 0.11 (0.06)

No SSB: -1.75 (0.6), -3.34 (0.75)

**Change over time, between groups:** 6mo

**P<0.001**

**Waist Circumference % of change**

**Change over time, within group:** 3mo, 6mo

ASB: -1.56 (0.46), -1.23 (0.58)

No SSB: -2.45 (0.44), -4.07 (0.54)

**Change over time, between groups:** 6mo

**P<0.001**

**Hip Circumference % of change**

**Change over time, within group:** 3mo, 6mo

ASB: -0.71 (0.35), -0.35 (0.46)

No SSB: -1.63 (0.30), -3.00 (0.44)

**Change over time, between groups:** 6mo

P=NS

**Resistance/Height % of change**

**Change over time, within group:** 3mo, 6mo

ASB: -0.85 (1.49), 2.00 (1.38)

No SSB: -1.92 (1.61), -2.12 (0.95)

**Change over time, between groups:** 6mo

**P=0.02**

**Phase angle % of change**

**Change over time, within group:** 3mo, 6mo

ASB: 5.57 (1.20), 4.92 (1.28)

No SSB: 4.88 (0.76), 8.40 (0.85)

**Change over time, between groups:** 6mo

P=NS

**TEI adjusted:** Yes (all participants were on individualized isocaloric diets)

**Energy Intake, % change from baseline EI, Mean (SD)**

**EI, change over 6mo within group:**

No SSB: -16.88 (2068)

Control: -6.92 (3.46)

**Change over time, between groups:** P=0.01

**Confounders accounted for:**

- Key confounders: (No baseline differences) sex, age, anthropometry at baseline
- Other factors considered: total energy intake, medications

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity, SES, physical activity, smoking
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, supplements, alcohol

**Additional model adjustments:** N/A

**Limitations:**

- Not all key confounders accounted for

**Funding Sources:**

Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<b>PROSPECTIVE COHORT STUDIES</b>			
<p><b>Bes-Rastrollo, 2008<sup>9</sup></b>  <b>Prospective Cohort Study, Nurses' Health Study II, United States</b>  Baseline N=116671, Analytic N=50026 (Attrition: 57%); Power: NR</p> <p><b>Recruitment:</b> convenience sample of nurses from 14 states</p> <p><b>Participant characteristics: Women</b></p> <ul style="list-style-type: none"> <li>Total energy intake, kcal/d, Mean (SE): 1771 (522)</li> <li>Sex (female): 100%</li> <li>Age, y, Mean (SD): 36.5 (4.6)</li> <li>Race/ethnicity: NR</li> <li>SES: NR</li> <li>Anthropometrics, Mean (SD): BMI=24.2 (5.0); Weight, kg=65.9 (14.3)</li> <li>Physical activity, MET-h/wk, Mean (SD): 20.4 (26.4)</li> <li>Smoking: Current, 11.1%</li> </ul> <p><b>Summary of findings:</b>  Among women, greater 8-year change in low calorie caffeine free cola, but not low calorie cola, was associated with greater 8-year weight loss.</p>	<p><b>Exposure of interest:</b> Low calorie cola, Low calorie caffeine free cola</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Low calorie cola intake (categorical; tertiles) <ul style="list-style-type: none"> <li>Lowest tertile 8y change (ref)</li> <li>Highest tertile 8y change</li> </ul> </li> <li>Low calorie caffeine free cola (categorical; tertiles) <ul style="list-style-type: none"> <li>Lowest tertile 8y change (ref)</li> <li>Highest tertile 8y change</li> </ul> </li> </ul> <p>Other exposures: skim milk, milk, water, tea, decaffeinated coffee, coffee, tomato juice, caffeine free cola, cola, orange juice, apple juice, other carbonated beverages, punch</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Self-administered semi-quantitative FFQ; Represents intake during previous year</li> <li>At baseline, 8y follow-up</li> </ul> <p><b>Study beverage intake:</b> g/d, Mean (SD)</p> <ul style="list-style-type: none"> <li>Low-calorie carbonated soda: 223.5 (336.3)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, 8y follow-up</li> <li>Weight, self-reported through biennial questionnaires</li> </ul>	<p><u>Low calorie cola, categorical Weight</u>, Linear regression  8y change in weight by 8y change in intake, between group:  Lowest tertile (ref) vs Highest tertile: Data NR, P=NS</p> <p><u>Low calorie caffeine free cola, categorical Weight</u>, Linear regression  8y change in weight by 8y change in intake, between group:  <b>Lowest tertile (ref) vs Highest tertile: Data NR, P&lt;0.05</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: none</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  Postmenopausal hormone use, oral contraceptive use, changes in confounders between time periods</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Exposures were not well described</li> <li>Impact of missing data on analyses unclear</li> <li>Self-reported weight</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH; Spanish Ministry of Education; Fundacion Caja Madrid; Amigos de la Universidad de Navarra; AHA Established Investigator Award</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Duffey, 2012<sup>144</sup></b>  <b>Prospective Cohort Study, Coronary Artery Risk Development in Young Adults (CARDIA), United States</b>  Baseline N=5115, Analytic N=3524  (Attrition: 31%); Power: NR</p> <p><b>Recruitment:</b> from Birmingham, AL; Oakland, CA; Minneapolis, MN; and Chicago, IL</p> <p><b>Participant characteristics: young adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): ~63%</li> <li>• Age: ~25y</li> <li>• Race/ethnicity: Black ~62%</li> <li>• SES: High School ~35%, Some College ~39%, College ~32%</li> <li>• Anthropometrics: BMI ~24.5 kg/m<sup>2</sup>; Overweight ~23%, Obese ~10%</li> <li>• Physical activity: ~425 EU/wk</li> <li>• Smoking: Former ~15%; Current ~36%; Never ~67%</li> </ul> <p><b>Summary of findings:</b>  Young adults who consumed diet beverages at baseline (~25y) had lower risk of high waist circumference over 20y of follow up compared to diet beverage consumers. Diet beverage consumption did not significantly interact with dietary pattern to predict WC.</p>	<p><b>Exposure of interest:</b> Diet beverage intake (no calories)</p> <p><b>Comparators:</b> Diet beverage intake (categorical)</p> <ul style="list-style-type: none"> <li>• Consumer: consumed diet beverages</li> <li>• Non-consumer: did not consume diet beverages</li> </ul> <p>Other exposure measures: N/A</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Validated CARDIA Diet History questionnaire (interviewer-administered), asks about general dietary practices</li> <li>• Quantitative diet history, represents consumption over the previous month</li> <li>• Both at baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Diet beverage consumers at baseline: 22%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, and 2, 5, 7, 10, 15, and 20y follow-up</li> <li>• Waist circumference (WC) measured at the minimum abdominal girth by trained technicians; average of 2 measures used for analysis</li> <li>• High WC: &gt;35 in (&gt;88 cm) for women or &gt;40 in (&gt;102 cm) for men</li> </ul>	<p><b>High WC</b>, Proportional hazards, HR (95% CI)  Consumer (ref) vs.  <b>Non-consumer: 0.84 (0.73, 0.97), P&lt;0.05</b></p> <p><b>High WC</b>, Proportional hazards, HR (95% CI)  Western Consumers (ref) vs.  Western Nonconsumers: 0.85 (0.70, 1.04)  Prudent Consumers: 0.93 (0.73, 1.17)  Prudent Non-consumers: 0.78 (0.62, 0.97)  P-interaction: 0.943</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: N/A</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>  CARDIA study center; dietary pattern</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Attrition 31% without information on non-completers</li> <li>• Exposure measured only at baseline</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  NIH; UNC-CH Center for Environmental Health and Susceptibility; UNC-CH Clinic Nutrition Research Center; Carolina Population Center; University of Alabama at Birmingham, Field Center; University of Minnesota, Field Center; Northwestern University, Field Center; Kaiser Foundation Research Institute (NHLBI)</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Ferreira-Pêgo, 2016<sup>68</sup></b>  <b>Prospective analyses of RCT, PREDIMED (PREvención con Dieta MEDiterránea), Spain</b>  Baseline N= 2094; Analytic N=1,868; Attrition: 11%; Power: NR</p> <p><b>Recruitment:</b> participants were selected from all of the PREDIMED recruitment centers with biochemical determinations available for a follow-up of ≥2 y; all participants were at high risk of CVD due to the presence of T2D or ≥3 risk factors: current smoking, hypertension, high LDL cholesterol, low HDL cholesterol, overweight or obese, or family history of premature CVD, but did not have MetSyn</p> <p><b>Participant characteristics: adults, high risk for CVD</b></p> <ul style="list-style-type: none"> <li>• Total energy intake, kcal/d, Mean (SD): 2322.6 (~530)</li> <li>• Sex (female): 52.5%</li> <li>• Age: ~67y (~6y)</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI: 28.3 (~3.5)</li> <li>• Physical activity: Leisure time MET-min/d: ~274 (252)</li> <li>• Smoking: ~58%: Never; ~17% Current; ~26% Former</li> </ul> <p><b>Summary of findings:</b>  In a sample of older adults at high-risk for CVD, the highest level of LNCSB consumption (&gt;5 serv/wk) was associated with greater risk of abdominal obesity over a follow-up period of ≥2y.</p>	<p><b>Exposure of interest:</b> Artificially sweetened beverages (LNCSBs; 1 svg=200mL</p> <p><b>Comparators:</b> Artificially sweetened beverages, categorical</p> <ul style="list-style-type: none"> <li>• &lt;1 serv/wk (Ref)</li> <li>• 1-5 serv/wk</li> <li>• &gt;5 serv/wk</li> </ul> <p>Other exposures measured: Natural fruit juices, bottled fruit juices, SSBs</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated FFQ assessing habitual intake for previous year</li> <li>• At baseline, annually</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• During follow up: Mean 17.1 mL/d</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• Baseline, yearly during follow-up period of ≥2y</li> <li>• Weight: measured by trained personnel with calibrated scales</li> <li>• Height: measured by trained personnel with a wall-mounted stadiometer.</li> <li>• Waist circumference measured using an anthropometric tape midway between the lower rib and the superior border of the iliac crest</li> <li>• Abdominal obesity: waist circumference ≥88cm in women and ≥102 cm in men</li> </ul>	<p><b>Abdominal obesity</b>, Multivariable time-dependent Cox proportional regression, HR (95% CI)</p> <p><b>LNCSBs:</b>  &lt;1 serv/wk: Ref  1-5 serv/wk: 0.91 (0.65, 1.28)  <b>&gt;5 serv/wk: 1.82 (1.13, 2.92)</b>  P for trend: 0.039</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, alcohol (overall alcohol intake &amp; alcohol squared in grams per day)</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements,</li> </ul> <p><b>Additional model adjustments:</b>  Intervention group, average consumption during the follow-up of dietary variables as continuous variables, prevalence of MetS components at baseline)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• No information on whether or not amount of missing data varied across exposure groups</li> <li>• Follow-up time differs among participants</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  Spanish Ministry of Health, the Thematic Network, FEDER (European Regional Development Fund), the Centre Català de la Nutrició de l'Institut d'Estudis Catalans, and the Fundació "LaMarat" o de TV3"</p>

**Fowler, 2015<sup>104</sup>****Prospective Cohort Study, San Antonio Longitudinal Study of Aging (SALSA), United States**

Baseline N=749, Analytic N=466;  
Attrition: 38%; Power: NR

**Recruitment:** from the San Antonio Heart Study (SAHS) cohort, a community-based prospective study of cardiovascular risk factors among Mexican Americans and European Americans, conducted in San Antonio, Texas, between 1979 and 1996

**Participant characteristics: older adults (65+yo)**

- Total energy intake: NR
- Sex (female): ~60%
- Age: ~69y
- Race/ethnicity: ~50% Mexican-American; ~50% European-American
- SES: ~35% suburb residents; ~20% barrio residents
- Anthropometrics: BMI ~29 kg/m<sup>2</sup>; WC ~100cm; ~78% ovwt/obese
- Physical activity: leisure time energy expenditure ~1800 kcal/wk
- Smoking: currently smoking ~10%

**Summary of findings:**

In adults over 65y, not consuming diet sodas was associated with loss in BMI over time, whereas consuming diet soda/d was not associated with a change in BMI. There was a significant trend indicating greater diet soda intake was associated with increasing waist circumference over time.

**Exposure of interest:** Diet soda intake (sugar-free soda)

**Comparators:** Diet soda intake, categorical

- None/Non-users: 0-0.05 diet sodas/d
- Occasional users: >0 but <1 soda/d
- Daily users: ≥1 soda/d

Other exposure measures: regular soda

**Exposure assessment method and timing:**

- Questionnaire; represents weekly intake; non-validated
- At baseline and beginning of each follow-up interval (~7y, 8.5, 10y from baseline)

**Diet soda intake:**

- None/Non-users: 0-0.05 diet sodas/d, n=255
- Occasional users: >0 but <1 soda/d, n=89
- Daily users: ≥1 soda/d, n=40

**Outcome assessment methods/timing:**

- At baseline, 3 follow-ups: FU1 ~7y, FU2 ~1.5y; FU3 ~1.5y; total ~9.4y (range 4.5-12.5y)
- Height and weight measured
- BMI calculated as kg/m<sup>2</sup>
- Waist Circumference (WC) measured in cm at the level of the umbilicus

**Change in BMI, kg/m<sup>2</sup>, over interval.**

By diet soda consumption category, Mean (95% CI)

None: -0.41 (-0.57, -0.25) (ref)  
>0 and <1: -0.11 (-0.38, 0.16)

**≥1: 0.05 (-0.35, 0.45), P<0.043**  
**P-trend= 0.049**

**Change in WC, cm, over interval.** By diet soda consumption category, Mean (95% CI)

**None/Non-User:** 0.77 (0.29, 1.23) (ref)  
**Occasional (>0 and <1):** 1.76 (0.96, 2.57)

**Daily (≥1): 3.04 (1.82, 4.26), P<0.001**  
**P-trend= 0.002**

**SUBGROUP ANALYSES:**

N denotes number of person-years

**Overall: P-diff<0.001**

**None (N=2405): 0.77 (0.29, 1.23)**

**Any (n=1301): 2.11 (1.45, 2.76)**

**Men: P-diff=0.002; P-interaction=0.154**

**None (n=955): 0.29 (-0.47, 1.05)**

**Any (n=526): 2.31 (1.30, 3.32)**

**Women: P-diff=0.139**

**None (n=1450): 1.09 (0.47, 1.71)**

**Any (n=774): 1.92 (1.05, 2.79)**

**Mex-Amer: P-diff=0.150; P-**

**interaction=0.439**

**None (n=1299): 0.76 (0.07, 1.46)**

**Any (n=517): 1.71 (0.67, 2.75)**

**European-American: P-diff=0.005**

**None (N=1106): 0.80 (0.10, 1.49)**

**Any (N=784): 2.40 (1.55, 3.25)**

**BMI<25: P-diff=0.833**

**None (N=623): 1.70 (0.68, 2.72)**

**Any (N=205): 1.92 (0.10, 3.74)**

**BMI 25-30: P-diff=0.067; P-**

**interaction<0.001**

**None (N=1076): 1.19 (0.55, 1.84)**

**Any (N=575): 2.24 (1.38, 3.10)**

**BMI≥30: P-diff=0.031; P-**

**interaction<0.001**

**None (N=701): -0.53 (-1.68, 0.62)**

**Any (N=512): 1.53 (0.19, 2.87)**

**TEI adjusted:** No

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking
- Other factors considered: N/A

**Confounders NOT accounted for:**

- Key confounders: N/A
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:**

Diabetes, length of follow-up interval

**Limitations:**

- Exposure data collection tool not validated
- No preregistered data analysis plan

**Funding sources:**

NIA, NIDDK; NCRR; CTSA

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Fresan, 2016<sup>22</sup></b>  <b>Prospective Cohort Study, SUN Cohort, Spain</b>            Baseline N=17,984, Analytic N=15,765 (Attrition: 12%); Power: NR</p> <p><b>Recruitment:</b> Convenience sample of university graduates</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake, Mean (SD): ~2342 kcal/d</li> <li>Sex (female): 59.8%</li> <li>Age, Mean (SD): 37.9y (11.7)</li> <li>Race/ethnicity: NR</li> <li>SES: University graduate 100%</li> <li>Anthropometrics, Mean (SD): BMI, 23.49 (3.5)</li> <li>Physical activity, Mean (SD): ~21.7 MET-h/wk</li> <li>Smoking: Current smoker 21.6%, Former smoker 28.4%</li> </ul> <p><b>Summary of findings:</b>            Replacement of diet soda with water was not significantly associated with incidence of obesity or 4y weight change in adults.</p>	<p><b>Exposure of interest:</b> Diet soda beverages (1svg = 200mL)</p> <p><b>Comparators:</b> Substituting water for diet soda (continuous; svg/d water increase/svg/d decrease diet soda)</p> <p>Other exposures: Skim milk, reduced-fat milk, whole milk, milk shakes, SSSBs, regular coffee, decaffeinated coffee, fresh orange juice, fresh non-orange juice, bottled juice, water</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Semi-quantitative FFQ previously validated in Spain; Represents intake during previous year</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Diet soda beverages: Mean~0.8 svg/wk</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline, every 2y</li> <li>BMI from self-reported weight and height</li> <li>Obesity defined as BMI <math>\geq 30</math> kg/m<sup>2</sup></li> </ul>	<p><b>Substitution of 1 svg/d water for 1 svg/d diet soda, continuous Obesity</b>, OR (95% CI), logistic regression            0.91 (0.80, 1.04)  <b>4y Weight change</b>, g, Mean (95% CI), linear regression            -86 (-300, 129)</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: race/ethnicity, SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol</li> </ul> <p><b>Additional model adjustments:</b>            Personal history of obesity, family history of obesity, following a special diet, adherence to Mediterranean dietary pattern, snacking between meals, weight change in past 5y</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Two key confounders not accounted for</li> <li>Selection into study may have been related to exposure and outcome</li> <li>Weight self-reported</li> <li>No a priori protocol to compare analyses</li> </ul> <p><b>Funding sources:</b>            Spanish Ministry of Health; Navarra Regional Government; University of Navarra</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Gearon, 2018</b><sup>106</sup></p> <p><b>Prospective Cohort Study, Melbourne Collaborative Cohort Study (MCCS), Australia</b></p> <p>Analytic N=7894; Attrition: NR (Attrition in main analyses of cohort was ~35%); Power: NR</p> <p><b>Recruitment:</b> using telephone books and electoral rolls, as well as community announcements and advertisements</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 61%</li> <li>• Age: ~46y (Range 27-80y, focused on 40-69y)</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI, Women ~25, Men ~26</li> <li>• Physical activity: leisure time score ~4</li> <li>• Smoking: Never smoker, Women ~62%, Men ~52%</li> </ul> <p><b>Summary of findings:</b></p> <p>For women and men, consuming 1 or more diet soft drinks per month, compared to less than 1, was significantly associated with greater increases in BMI 13 years later.</p>	<p><b>Exposure of interest:</b> Diet soft drink</p> <p><b>Comparators:</b> categorical</p> <ul style="list-style-type: none"> <li>• &lt;1/mo</li> <li>• ≥ 1/mo</li> </ul> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• FFQ designed for the study; based on frequency, not amount; not validated</li> <li>• At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Soda intake:</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline and 13y follow-up</li> <li>• Weight and WC measured by practitioner</li> <li>• Height measured by practitioner at baseline only</li> </ul>	<p><b>BMI change over 13y,</b> Diet soft drink &lt;1/mo vs ≥ 1/mo, Linear regression, <math>\beta</math> (95% CI)</p> <p><b>Women: 0.52 (0.38, 0.67), P&lt;0.05</b></p> <p><b>Men: 0.28 (0.15, 0.43), P&lt;0.05</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: age, smoking</li> <li>• Other factors considered: alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, race/ethnicity, SES, anthropometry at baseline, physical activity</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b> none</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Bias due to missing data can't be determined</li> <li>• Exposure data only measured at baseline</li> <li>• Exposure classified by frequency not amount</li> <li>• Exposure data collection tool not validated</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>NHLBI; NCI</p>

**Hinkle, 2019<sup>145</sup>**

**Prospective Cohort Study, Diabetes & Women's Health (DWH), Denmark**

Baseline N=790, Analytic N=607  
(Attrition: 23%); Power: NR

**Recruitment:** women with gestational DM during index pregnancy of Danish National Birth Cohort (DNBC)

**Participant characteristics: women with prior gestational DM**

- Total energy intake: ~2400 kcal/d
- Sex (female): 100%
- Age: ~31y
- Race/ethnicity: NR
- SES: ≥High school education, 33%
- Anthropometrics: Pre-pregnancy BMI ~27 kg/m<sup>2</sup>
- Physical activity: MVPA ~0 MET-h/wk
- Smoking: 26% Smokers

**Summary of findings:**

In women with prior gestational diabetes mellitus, artificially sweetened beverage intake was not significantly associated with BMI, waist circumference, visceral adipose tissue, or risk of obesity at 9-16y follow-up.

**Exposure of interest:** Artificially sweetened beverages (ASBs included carbonated and noncarbonated sources, such as diet soda pop/Coca Cola without sugar, diet/light lemonade without sugar); 1 svg = 250 g

**Comparators:** ASB intake (categorical):

- <1 svg/mo (ref)
- 1-4 svg/mo
- 2-6 svg/wk
- ≥1 svg/d

**Exposure assessment method and timing:**

- Validated semi-quantitative FFQ; represents habitual dietary intake during previous month (DNBC) or year (DWH)
- At baseline (25wk gestation during DNBC 1996-2002), and at 9-16y follow-up (during DWH, 2012-2014)

**Study beverage intake:** ≥2 svg/wk

- ASB intake during pregnancy: 30%
- ASB intake at follow-up: 36%

**Outcome assessment methods/timing:**

- At 9-16y follow-up (2012-2014)
- Height and weight measured twice according to standardized protocol
- BMI calculated as kg/m<sup>2</sup>
- Waist circumference (WC) measured twice midway between lowest rib and iliac crest
- Abdominal visceral adipose tissue measured in subset of women (n=192) using whole-body DXA and estimated using enCORE software
- Obesity: BMI>30 kg/m<sup>2</sup>

**BMI.** Linear regression, % difference (95% CI)

*ASB in pregnancy* (n=606);

<1 svg/mo: ref

1-4 svg/mo: 1.5 (-1.9, 5.1)

2-6 svg/wk: 2.7 (-0.4, 5.9)

≥1 svg/d: 1.0 (-2.9, 5.0)

P-trend: 0.79

*Habitual ASB (in pregnancy and f/u)* (n=606)

≤4 svg/mo (preg and f/u): ref

≤4/mo (preg) and ≥2/mo at f/u: 1.5 (-2.7, 5.9)

≥2/wk (preg) and ≤4/mo at f/u: 3.5 (-0.2, 7.3)

≥2 svg/wk (preg and f/u): 1.5 (-1.7, 4.8)

**WC.** Linear regression, % difference (95% CI) *ASB in pregnancy* (n=606);

<1 svg/mo: ref

1-4 svg/mo: 2.0 (-0.5, 4.5)

**2-6 svg/wk: 2.6 (0.3, 4.9)**

≥1 svg/d: 1.6 (-1.1, 4.5)

P-trend: 0.40

*Habitual ASB (in pregnancy and f/u)* (n=606)

≤4 svg/mo (preg and f/u): ref

≤4/mo (preg) and ≥2/mo (f/u): -0.8 (-3.2, 1.6)

≥2/wk (preg) and ≤4/mo (f/u): 1.7 (-1.4, 4.9)

≥2 svg/wk (preg and f/u): 1.0 (-1.2, 3.3)

**Visceral Adipose Tissue.** Linear regression, % difference (95% CI)

*ASB in pregnancy* (n=192)

<1 svg/mo: ref

1-4 svg/mo: 27.6 (-14.4, 90.3)

2-6 svg/wk: 15.9 (-16.7, 61.4)

≥1 svg/d: 18.7 (-20.7, 77.7)

P-trend: 0.54

*Habitual ASB (in pregnancy and f/u)* (n=192)

≤4 svg/mo (preg and f/u): ref

≤4/mo (preg) and ≥2/mo (f/u): -0.2 (-30.8, 43.7)

≥2/wk (preg) & ≤4/mo (f/u): 13.6 (-25.0, 72.1)

≥2 svg/wk (preg and f/u): 3.7 (-26.4, 46.2)

**Obesity.** Poisson regression, RR (95% CI)

*ASB in pregnancy* (n=606);

**TEI adjusted:** No

**Confounders accounted for:**

- Key confounders: sex, age, SES, anthropometry at baseline, physical activity, smoking
- Other factors considered: N/A

**Confounders NOT accounted for:**

- Key confounders: race/ethnicity
- Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements, alcohol

**Additional model adjustments:**

Parity, Alternative Healthy Eating Index-2010, intake of tea and coffee, pre-pregnancy chronic diseases at the index pregnancy

**Limitations:**

- Not all key confounders accounted for
- Follow-up and start of exposure differ among participants
- No preregistered data analysis plan

**Funding sources:**

NICHD; March of Dimes Birth Defects Foundation; Innovation Fund Denmark; Health Foundation; Heart Foundation; European Union; Danish Diabetes Academy supports by Novo Nordisk Foundation

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
		<p>&lt;1 svg/mo: ref</p> <p>1-4 svg/mo: 1.20 (0.87, 1.64)</p> <p>2-6 svg/wk: 1.43 (1.13, 1.82)</p> <p>≥1 svg/d: 1.18 (0.89, 1.57)</p> <p>P-trend: 0.50</p> <p><i>Habitual ASB (in pregnancy and f/u)</i></p> <p>(n=606)</p> <p>≤4 svg/mo (preg and f/u): ref</p> <p>≤4/mo (preg) and ≥2/mo (f/u): 1.18 (0.88, 1.59)</p> <p>≥2/wk (preg) and ≤4/mo (f/u): 1.41 (0.98, 2.02)</p> <p>≥2 svg/wk (preg and f/u): 1.37 (1.04, 1.81)</p>	

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Ma, 2016<sup>118</sup></b>  <b>Prospective Cohort Study, Third Generation cohort of the Framingham Heart Study, United States</b>  Analytic N=1003 (Attrition: NR); Power: NR</p> <p><b>Recruitment:</b> mail to children of the Offspring Cohort</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>Total energy intake: ~1900 kcal/d</li> <li>Sex (female): 45%</li> <li>Age: Mean=45.3y</li> <li>Race/ethnicity: 99.7% White</li> <li>SES: NR</li> <li>Anthropometrics: BMI ~27.4 kg/m<sup>2</sup></li> <li>Physical activity: Score ~37.2</li> <li>Smoking: 9% Current smoker</li> </ul> <p><b>Summary of findings:</b>  In adults, diet soda intake was not significantly associated with changes in body weight at 6y follow-up.</p>	<p><b>Exposure of interest:</b> Diet soda intake (low-calorie cola; low-calorie, caffeine-free cola; other low-calorie carbonated beverage; "did not include all consumption of low calorie and artificially sweetened, noncarbonated beverages")</p> <p><b>Comparator:</b> Diet soda intake (categorical):</p> <ul style="list-style-type: none"> <li>Non-consumers (none to &lt;1 svg/mo): Median 0 svg/wk</li> <li>Occasional consumers (1 svg/mo to &lt;1 svg/wk): Median 0.5 svg/wk</li> <li>Frequent consumers (1 svg/wk to 1 svg/d): Median 3 svg/wk</li> <li>Daily consumers (≥1 svg/d): 12 svg/wk</li> </ul> <p>Other exposure measures: SSB</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Harvard semi-quantitative FFQ (validated)</li> <li>At baseline</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>Diet soda intake: 50% Non-consumers, 13% Occasional consumers, 22% Frequent consumers, 15% Daily consumers</li> </ul> <p>Note: intake also stratified by sex in paper</p> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>At baseline (2002-2005), ~6y follow-up (2008-2011)</li> <li>Height measured to nearest ¼ inch using vertical ruler</li> <li>Weight measured with light clothes and rounded to nearest 0.5 pound</li> <li>BMI calculated as kg/m<sup>2</sup></li> </ul>	<p><b>Weight</b>, kg, Linear regression, <math>\beta</math> (95% CI)  <b>Change per frequency of Diet Soda intake:</b>  Non-consumers: 2.8 (2.2, 3.3)  Occasional consumers: 1.6 (0.5, 2.7)  Frequent consumers: 1.7 (0.8, 2.5)  Daily consumers: 2.7 (1.7, 3.8)  P trend = 0.85  <b>P interaction (Sex) = 0.01</b>  P interaction (BMI) = 0.99  P interaction (T2DM) = 0.57</p> <p><b>MEN</b>  Non-consumers: 2.5 (1.8, 3.2)  Occasional consumers: 2.0 (0.5, 3.5)  Frequent consumers: 2.8 (1.7, 4.0)  Daily consumers: 3.7 (2.3, 5.0)  P trend = 0.10</p> <p><b>WOMEN</b>  Non-consumers: 3.3 (2.4, 4.2)  Occasional consumers: 1.1 (-0.6, 2.7)  Frequent consumers: 0.6 (-0.6, 1.8)  Daily consumers: 1.5 (-0.1, 3.0)  P trend = 0.11</p> <p><u><b>Data on change in visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) are also included in the paper if relevant</b></u></p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, (race/ethnicity), anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: total energy intake, supplements, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES</li> <li>Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications</li> </ul> <p><b>Additional model adjustments:</b>  Saturated fat intake, SSB intake, whole grain, fruit, vegetable, coffee, nuts, and fish</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>Not all key confounders accounted for</li> <li>Follow-up time differs among participants</li> <li>Exposure measured at baseline only</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>  NHLBI</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Mozaffarian, 2011<sup>42</sup></b>  <b>Prospective Cohort Study, Nurses Health Study (NHS) + NHS II + Health Professionals Follow-Up Study (HPS), United States</b>  <i>NHS</i>: Baseline N=121,700 Analytic N=50,013 (Attrition: 58.9%); Power: NR  <i>NHS II</i>: Baseline N=116,671 Analytic N=52,987 (Attrition: 54.6%); Power: NR  <i>HPS</i>: Baseline N=51,529 Analytic N=21,988 (Attrition: 57.3%); Power: NR</p> <p><b>Recruitment:</b> professional organizations or from occupation mailing house lists</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): NHS and NHS II 100%, HPS 0%</li> <li>• Age, y, Mean (SD): NHS 52.2 (7.2), NHS II 37.5 (4.1), HPS 50.8 (7.5)</li> <li>• Race/ethnicity: primarily white</li> <li>• SES: primarily educated</li> <li>• Anthropometrics, Mean (SD): BMI (kg/m<sup>2</sup>), NHS 23.7 (1.4), NHS II 23.0 (2.7), HPS 24.7 (1.1)</li> <li>• Physical activity, MET-hr/wk, Mean (SD): NHS 14.8 (9.9), NHS II 21.6 (25.9), HPS 22.9 (15.1)</li> <li>• Smoking: Never smoker 53%, Past smoker 33%, Current smoker 13%, Missing 1%</li> </ul> <p><b>Summary of findings:</b>  In adults, diet soda intake was significantly associated with weight loss.</p>	<p><b>Exposure of interest:</b> Diet soda intake ("low-calorie cola with caffeine", "low-calorie caffeine-free cola", and "other low-calorie beverages")</p> <p><b>Comparators:</b> Diet soda intake (continuous; svg/d)</p> <p>Other exposure measures: milk, SSBs, fruit juice</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated questionnaire; represents usual dietary intake</li> <li>• At baseline, every 4y over 12- to 20-y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Diet soda intake, svg/d, Mean (SD): NHS 0.5 (0.4), NHS II 1.0 (1.3), HPS 0.5 (0.5)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, and every 2y over 12- to 20-y follow-up</li> <li>• Weight was collected via self-report from questionnaire</li> </ul>	<p><b>Weight</b>, lb, Linear regression, <math>\beta</math> (95% CI)  <b>Change per svg/d increase:</b>  <i>NHS</i>: -0.04 (-0.10, 0.03), P=NS  <i>NHS II</i>: <b>-0.10 (-0.17, -0.03), P&lt;0.001</b>  <i>HPS</i>: <b>-0.21 (-0.30, -0.12), P&lt;0.001</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  television watching, sleep duration, dietary variables (fruits, vegetables, whole-fat and low-fat dairy, potato chips, potatoes/fries, whole grains, refined grains, sweets and desserts, processed and unprocessed meats, trans fat, fried foods at and away from home)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Weight was self-reported</li> </ul> <p><b>Funding sources:</b>  NIH; Searle Scholars Program</p>



Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Nettleton, 2009<sup>149</sup></b>  <b>Prospective Cohort Study, Multi-Ethnic Study of Atherosclerosis (MESA), United States</b>            Baseline N=5011, Analytic N=2428 (Attrition: 52%); Power: NR</p> <p><b>Recruitment:</b> six field centers (Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; New York, New York; Los Angeles County, California; and St. Paul, Minnesota)</p> <p><b>Participant characteristics: older adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~1650 kcal/d</li> <li>• Sex (female): 53%</li> <li>• Age: ~61y (45-84y)</li> <li>• Race/ethnicity: 43% White, 23% African American, 21% Hispanic, 12% Chinese</li> <li>• SES: 85% High school degree</li> <li>• Anthropometrics: BMI ~28 kg/m<sup>2</sup></li> <li>• Physical activity: Active leisure ~2650 MET-min/wk</li> <li>• Smoking: 14% Current</li> </ul> <p><b>Summary of findings:</b>            In adults, diet soda consumption ≥1/d was associated with greater risk of high waist circumference over time; however, this was attenuated when controlling for baseline waist circumference.</p>	<p><b>Exposure of interest:</b> Diet soda intake (diet soda drinks, unsweetened mineral water)</p> <p><b>Comparators:</b> Diet soda intake (categorical):</p> <ul style="list-style-type: none"> <li>• Rare/never (Median 0.0 svg/d)</li> <li>• More than rare/never but &lt;1 svg/wk (Median 0.1 svg/d)</li> <li>• ≥1 svg/wk to &lt;1 svg/d (Median 0.4 svg/d)</li> <li>• ≥1 svg/d (Median 2.5 svg/d)</li> </ul> <p>Other exposure measures: SSB</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated FFQ; represents frequency and serving size</li> <li>• At baseline (2000-2002)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Diet soda intake: Never, 59%; ≥1 svg/d, 14%</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline (2000-2002), and three follow-ups (2002-2003, 2004-2005, 2005-2007)</li> <li>• BMI calculated from measured weight in kg divided by square of height in meters</li> <li>• Waist circumference (WC) measured at umbilicus using standard tape measure; high WC defined as ≥102 cm in men or ≥88 cm in women</li> </ul>	<p><b>High WC</b>, Cox proportional hazard, HR (95% CI)            Rare/never (n=1544, ref) vs            &gt;never to &lt;1 svg/wk (n=208): 1.13 (0.82, 1.57)            ≥1 svg/wk-&lt;1 svg/d (n=602): 1.22 (0.95, 1.55)  <b>≥ 1 svg/d (n=449): 1.59 (1.23, 2.07)</b></p> <p><i>When adjusting for baseline WC:</i>            Rare/never (ref) vs            ≥ 1 svg/d: 1.18 (0.96, 1.44)</p>	<p><b>TEI adjusted:</b> Yes</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, race/ethnicity, SES, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: total energy intake, supplements</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: N/A</li> <li>• Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, alcohol</li> </ul> <p><b>Additional model adjustments:</b>            Study site</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Exposure data only measured at baseline</li> <li>• Exposure not well-defined</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding source:</b>            NHLBI</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Pan, 2013<sup>46</sup></b>  <b>Prospective Cohort Study, Nurses Health Study (NHS) + NHS II + Health Professionals Follow-Up Study (HPS), United States</b>  <i>NHS</i>: Baseline N=121,700 Analytic N=50,013 (Attrition: 58.9%); Power: NR  <i>NHS II</i>: Baseline N=116,671 Analytic N=52,987 (Attrition: 54.6%); Power: NR  <i>HPS</i>: Baseline N=51,529 Analytic N=21,988 (Attrition: 57.3%); Power: NR</p> <p><b>Recruitment:</b> professional organizations or from occupation mailing house lists</p> <p><b>Participant characteristics: adults</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: NR</li> <li>• Sex (female): 82%</li> <li>• Age: Mean~47y</li> <li>• Race/ethnicity: primarily white</li> <li>• SES: primarily educated</li> <li>• Anthropometrics: Overweight 31%, Obesity 17%, BMI: Mean~25 kg/m<sup>2</sup></li> <li>• Physical activity: Mean~18 MET-hr/wk</li> <li>• Smoking: Never smoker 54%, Past smoker 33%, Current smoker 13%</li> </ul> <p><b>Summary of findings:</b>  In adults, when stratified by baseline BMI, increasing intakes of diet beverages was significantly associated with weight loss.</p>	<p><b>Exposure of interest:</b> Diet beverage intake ("low-calorie cola with caffeine", "low-calorie caffeine-free cola", and "other low-calorie beverages")</p> <p><b>Comparators:</b> Diet beverage intake (continuous; svg/d)</p> <p>Other exposure measures: milk, water, SSBs, fruit juice, coffee, tea</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>• Validated FFQ; represents usual intake of foods and beverages</li> <li>• At baseline, every 4y over 16- to 20-y follow-up</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Diet beverage intake, svg/d, Mean (5<sup>th</sup>-95<sup>th</sup>%): <i>NHS</i> 0.52 (0-2.5), <i>NHS II</i> 1.06 (0-4.5), <i>HPS</i> 0.51 (0-2.5)</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline, and every 2y over 16- to 20-y follow-up</li> <li>• Weight was collected via self-report from questionnaire</li> </ul>	<p><b>Weight</b>, kg, Linear regression, <math>\beta</math> (95% CI)  <b>Change per svg/d increase:</b>  <i>NHS</i>: -0.11 (-0.15, -0.08)  <i>NHS II</i>: -0.07 (-0.10, -0.03)  <i>HPS</i>: -0.14 (-0.18, -0.09)</p> <p><b>Stratified by age:</b> <math>\leq 50y</math>, <math>&gt;50y</math>  <b><i>NHS</i>: -0.19 (-0.26, -0.12), 0.13 (0.09, 0.18), P&lt;0.001</b>  <b><i>NHS II</i>: -0.09 (-0.13, -0.06), 0.13 (0.04, 0.22), P&lt;0.001</b>  <i>HPS</i>: -0.17 (-0.25, -0.09), -0.12 (-0.18, -0.06), P=0.07</p> <p><b>Stratified by BMI (kg/m<sup>2</sup>):</b> <math>&lt;25</math>, 25-29.9, <math>\geq 30</math>  <b><i>NHS</i>: -0.02 (-0.07, 0.02), -0.13 (-0.20, -0.07), -0.23 (-0.34, -0.12), P&lt;0.001</b>  <i>NHS II</i>: 0.00 (-0.03, 0.04), -0.11 (-0.17, -0.05), -0.07 (-0.16, 0.02), P=0.09  <b><i>HPS</i>: -0.02 (-0.08, 0.04), -0.14 (-0.21, -0.08), -0.26 (-0.44, -0.08), P&lt;0.001</b></p>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: sugar, protein, alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES</li> <li>• Other factors considered: total energy intake, timing, temporal use, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Television watching, dietary variables (fruits, vegetables, whole grain, refined grain, potatoes, potato chips, red meat, other dairy products, sweets and deserts, nuts, fried foods, and trans fat), other beverage variables</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Weight was self-reported</li> </ul> <p><b>Funding sources:</b>  NIH</p>

Qi, 2012<sup>127</sup>

**Prospective Cohort Study, Nurses Health Study (NHS) + Health Professionals Follow-Up Study (HPFS) + Women's Genome Health Study (WGHS), United States**

NHS: Analytic N=6934 (Attrition: NR); Power: NR  
HPFS: Analytic N=4423 (Attrition: NR); Power: NR  
WGHS: Analytic N=21740 (Attrition: NR); Power: NR

**Recruitment:** professional organizations or from occupation mailing house lists

**Participant characteristics: adults**

- Total energy intake: ~1700 kcal/d
- Sex (female): 87%
- Age: Mean~51y
- Race/ethnicity: 100% European ancestry
- SES: all health professionals
- Anthropometrics: BMI: Mean~25 kg/m<sup>2</sup>
- Physical activity: Mean~16 MET-hr/wk
- Smoking: Current smoker ~9%

**Summary of findings:**

Artificially sweetened beverage intake was not associated with changes in BMI or incident obesity over time in adults with greater genetic predisposition of obesity.

[Note: Analyses first run in NHS & HPFS, then repeated in WGHS to replicate results. Exposure data used to predict prospective change in BMI in 4y chunks in NHS & HPFS. Genetic predisposition scores calculated based on obesity-related SNPs; each point of the genetic-predisposition score corresponded to one risk allele.]

**Exposure of interest:** Artificially sweetened beverage intake (caffeinated, caffeine-free, and noncarbonated low-calorie beverages)

**Comparators:** Artificially sweetened beverage intake (categorical; servings):

- <1 svg/mo
- 1-4 svg/mo
- 2-6 svg/wk
- ≥1 svg/d

Other exposure measures: SSB

Exposure assessment method and timing:

- Validated semi quantitative FFQ
- At baseline, and every 4y after for NHS and HPFS
- At baseline only for WGHS

**Study beverage intake:** svg/d, Mean

- Artificially sweetened beverage intake:
  - NHS: ~0.4
  - HPFS: ~0.5
  - WGHS: ~0.8

**Outcome assessment methods/timing:**

- NHS: At baseline, and every 4y follow-up assessment up to 18y
- HPFS: At baseline, and every 4y follow-up assessment up to 12y
- WGHS: At baseline, and 6y follow-up
- Height and weight were self-reported and highly correlated (0.97) with measured values in a sub-sample
- BMI calculated as kg/m<sup>2</sup>
- Obesity (BMI>30 kg/m<sup>2</sup>)

Data represent the difference in BMI for each increment of 10 risk alleles, stratified by beverage intake. **P for interaction (genetic predisposition score\*beverage intake)**

**Increase in BMI, per increment of 10 risk alleles, Linear regression,  $\beta$  (SE)**

NHS (n=6934)

<1 svg/mo: 1.42 (0.18)  
1-4 svg/mo: 1.25 (0.21)  
2-6 svg/wk: 1.39 (0.20)  
≥1 svg/d: 1.36 (0.27)  
P for interaction = 0.91

HPFS (n=4432)

<1 svg/mo: 0.95 (0.18)  
1-4 svg/mo: 0.76 (0.23)  
2-6 svg/wk: 0.45 (0.20)  
≥1 svg/d: 0.92 (0.29)  
P for interaction = 0.46

WGHS (n=21,740)

<1 svg/mo: 1.60 (0.15)  
1-4 svg/mo: 1.43 (0.25)  
2-6 svg/wk: 1.46 (0.16)  
≥1 svg/d: 1.63 (0.18)  
P for interaction = 0.81

**TEI adjusted:** Yes

**Confounders accounted for:**

- Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity, smoking
- Other factors considered: total energy intake, alcohol

**Confounders NOT accounted for:**

- Key confounders: SES
- Other factors considered: timing, temporal use, sugar, protein, fiber, energy density, medications, supplements

**Additional model adjustments:**

Source of genotyping data or eigenvectors derived from GWAS, time spent watching television (for NHS and HPFS), Alternative Healthy Eating Index score (for NHS and HPFS), and geographic region (for WGHS)

**Limitations:**

- Not all key confounders accounted for
- Weight and height self-reported
- No preregistered data analysis plan

**Funding sources:**

NIH; Merck Research Laboratories; American Heart Association; Harvard Glaucoma Center of Excellence; Amgen

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Schulze, 2004</b><sup>152</sup></p> <p><b>Prospective Cohort Study, Nurses' Health Study II, United States</b></p> <p>Baseline N=116671, Analytic N=51603; Attrition: 56%; Power: NR</p> <p><b>Recruitment:</b> nurses at study institution in 1989</p> <p><b>Participant characteristics: young and middle-aged women</b></p> <ul style="list-style-type: none"> <li>• Total energy intake: ~1800 kcal/d</li> <li>• Sex (female): 100%</li> <li>• Age: ~36y (24-44y)</li> <li>• Race/ethnicity: NR</li> <li>• SES: NR</li> <li>• Anthropometrics: BMI ~24.4 kg/m<sup>2</sup></li> <li>• Physical activity: ~19 METs/wk</li> <li>• Smoking: 12% Current</li> </ul> <p><b>Summary of findings:</b></p> <p>Women who increased their diet soft drink consumption had less weight gain at 4y follow-up compared to women who decreased their diet soft drink consumption.</p>	<p><b>Exposure of interest:</b> Diet soft drinks (low-calorie cola with caffeine, low-calorie caffeine-free cola, and other low-calorie beverages)</p> <p><b>Comparators:</b> Diet soft drink intake (categorical; change in drink frequency from 1991 to 1995):</p> <ul style="list-style-type: none"> <li>• Consistent ≤1/wk</li> <li>• Consistent ≥1/d</li> <li>• Increased (≤1/wk to ≥1/d)</li> <li>• Decreased (≥1/d to ≤1/wk)</li> <li>• Other</li> </ul> <p>Other exposure measures: SSB, juice, fruit punch</p> <p><b>Exposure assessment method and timing:</b></p> <ul style="list-style-type: none"> <li>• Validated semi-quantitative FFQ; represents intake over previous year</li> <li>• At baseline (1991), and 4y follow-up (1995)</li> </ul> <p><b>Study beverage intake:</b></p> <ul style="list-style-type: none"> <li>• Diet soft drink intake: NR</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>• At baseline (1991), and 4y follow-up (1995)</li> <li>• Height measured via self-report at baseline only</li> <li>• Weight measured via self-report</li> <li>• BMI calculated as kg/m<sup>2</sup></li> </ul>	<p><b>Weight gain, Per change in diet soft drink consumption from 1991-1995:</b></p> <p><b>Increased intake (≤1/wk to ≥1/d): 1.59 kg</b></p> <p><b>Decreased intake (≥1/d to ≤1/wk): 4.25 kg</b></p> <p><b>P&lt;0.001</b></p>	<p>TEI adjusted: No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: sex, age, anthropometry at baseline, physical activity, smoking</li> <li>• Other factors considered: alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>• Key confounders: race/ethnicity, SES</li> <li>• Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b></p> <p>Postmenopausal hormone use, oral contraceptive use, cereal fiber intake, total fat intake</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>• Not all key confounders accounted for</li> <li>• Attrition 56% without information on non-completers</li> <li>• Weight and height self-reported</li> <li>• No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b></p> <p>NIH; European Association for the Study of Diabetes/American Diabetes Association; German Academic Exchange Service (DAAD)</p>

Study and Population Characteristics	Intervention/Exposure, Comparator and Outcome(s)	Results	Total Energy Intake, Confounders, and Study Limitations
<p><b>Stern, 2017<sup>131</sup></b>  <b>Prospective Cohort Study, Mexican Teachers' Cohort, Mexico</b>  Baseline N=27992, Analytic N=11218 for weight and N=9294 for WC (Attrition: 60% weight, 67% WC); Power: NR</p> <p><b>Recruitment:</b> female teachers from Jalisco and Veracruz, Mexico</p> <p><b>Participant characteristics: Hispanic females living in Mexico</b></p> <ul style="list-style-type: none"> <li>Total energy intake: 1756 (614) kcal/d</li> <li>Sex (female): 100%</li> <li>Age: 43.3 (5.2) y; Range 25-64</li> <li>Race/ethnicity: 100% Hispanic</li> <li>SES: NR</li> <li>Anthropometrics: BMI 27.2 (4.4) kg/m<sup>2</sup>; 42% Overweight, 23% Obese</li> <li>Physical activity: High 34%, Medium 37%, Low 29%</li> <li>Smoking: Never 81%, Current 8%</li> </ul> <p><b>Summary of findings:</b>  In Hispanic females living in Mexico, changes in sugar-free soda consumption was not associated with changes in weight over a 2-yr period. An increase of 1 svg/d of sugar-free soda consumption was significantly associated with a decrease in waist circumference over a 2-yr period.</p>	<p><b>Exposure of interest:</b> Sugar-free soda</p> <p><b>Comparators:</b></p> <ul style="list-style-type: none"> <li>Sugar-free soda intake (continuous; svg/d):</li> <li>Sugar-free soda intake (categorical; svg/mo): <ul style="list-style-type: none"> <li>Decreased (&lt;-1 svg/mo)</li> <li>No change (-1 to +1 svg/mo)</li> <li>Increased (&gt;1 svg/mo)</li> </ul> </li> </ul> <p>Other exposure measures: sugar-sweetened soda</p> <p><u>Exposure assessment method and timing:</u></p> <ul style="list-style-type: none"> <li>Validated semi-quantitative FFQ; represents intake over previous year</li> <li>In 2006 and 2008</li> </ul> <p><b>Study beverage intake:</b> Mean (SD)</p> <ul style="list-style-type: none"> <li>Sugar-free soda: 0.1 (0.1) svg/wk</li> </ul> <p><b>Outcome assessment methods/timing:</b></p> <ul style="list-style-type: none"> <li>In 2006 and 2008</li> <li>Height (in cm) and weight (in kg) were self-reported</li> <li>Waist circumference (WC, in cm) was self-reported; participants were provided a plastic measuring tape and instructions to assess their WC</li> </ul>	<p><b>Weight, kg, Change from 2006–2008,</b> Linear regression, <math>\beta</math> (95% CI)  <b>Per 1 svg/d increase:</b> 0.0 (-1.3, 1.4), P=0.98  <b>Per change in svg/mo:</b></p> <ul style="list-style-type: none"> <li>No change (-1 to +1, n=7437): Ref</li> <li>Decreased (&lt;1, n=2270): -0.1 (-0.3, 0.1)</li> <li>Increased (&gt;1, n=1511): -0.2 (-0.4, 0.0)</li> </ul> <p><b>WC, cm, change from 2006–2008,</b> Linear regression, <math>\beta</math> (95% CI)  <b>Per 1 svg/d increase: -2.7 (-5.2, -0.1), P=0.04</b>  <b>Per change in svg/mo:</b></p> <ul style="list-style-type: none"> <li>No change (-1 to +1, n=6220): Ref</li> <li>Decreased (&lt;1, n=1856): -0.1 (-0.5, 0.3)</li> <li><b>Increased (&gt;1, n=1218): -0.7 (-1.1, -0.3)</b></li> </ul>	<p><b>TEI adjusted:</b> No</p> <p><b>Confounders accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: sex, age, race/ethnicity, anthropometry at baseline, physical activity, smoking</li> <li>Other factors considered: alcohol</li> </ul> <p><b>Confounders NOT accounted for:</b></p> <ul style="list-style-type: none"> <li>Key confounders: SES</li> <li>Other factors considered: total energy intake, timing, temporal use, sugar, protein, fiber, energy density, medications, supplements</li> </ul> <p><b>Additional model adjustments:</b>  Sugar-sweetened soda consumption, state of residency, oral contraceptive use, menopausal status, postmenopausal hormone therapy use, food and beverage intake (red meat, dairy, yogurt, fruit, vegetables, nuts, white bread, flour tortillas, corn tortillas, orange or grapefruit juice, and homemade sweetened beverages)</p> <p><b>Limitations:</b></p> <ul style="list-style-type: none"> <li>One key confounder not accounted for</li> <li>Attrition 60% without information on non-completers</li> <li>Weight, height, and waist circumference self-reported</li> <li>No preregistered data analysis plan</li> </ul> <p><b>Funding sources:</b>  AstraZeneca; Bloomberg Philanthropies (National Institute of Public Health in Mexico); Bernard Lown Scholars Program in Cardiovascular Health; American Institute of Cancer Research; Consejo Nacional de Ciencia y Tecnología; NIH</p>

**Table 30. Risk of bias for randomized controlled trials examining LNCSB consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>lxii, lxiii</sup>**

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Bonnet, 2018 <sup>142</sup>	Some Concerns	Some Concerns	Low	Some Concerns	Some Concerns
Madjd, 2015 <sup>147</sup>	Low	Some Concerns	Low	Low	Some Concerns
Madjd, 2018 <sup>148</sup>	Low	Some Concerns	Low	Low	Some Concerns
Peters, 2014 <sup>151</sup>	Some Concerns	Low	Some Concerns	Low	Low
Peters, 2016 <sup>150</sup>	Some Concerns	Low	Some Concerns	Low	Low
Vazquez-Duran, 2016 <sup>137</sup>	Low	Low	Low	Low	Low

<sup>lxii</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>lxiii</sup> Possible ratings of low, some concerns, or high determined using the "[Cochrane Risk-of-bias 2.0](#)" (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). *Cochrane Methods. Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). [dx.doi.org/10.1002/14651858.CD201601](https://doi.org/10.1002/14651858.CD201601).)

**Table 31. Risk of bias for prospective cohort studies examining LNCSB consumption and growth, size, body composition and risk of overweight and obesity in adults<sup>lxiv, lxv</sup>**

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Bes-Rastrollo, 2008 <sup>9</sup>	Serious	Low	Moderate	Low	Moderate	Moderate	Moderate
Duffey, 2012 <sup>144</sup>	Moderate	Low	Low	Moderate	Moderate	Low	Moderate
Ferreira-Pego, 2016 <sup>68</sup>	Serious	Moderate	Low	Moderate	Low	Low	Moderate
Fowler, 2015 <sup>104</sup>	Moderate	Low	Moderate	Low	Low	Low	Moderate
Fresan, 2016 <sup>22</sup>	Serious	Moderate	Low	Low	Low	Moderate	Moderate
Gearon, 2018 <sup>106</sup>	Serious	Moderate	Moderate	Moderate	Moderate	Low	Moderate
Hinkle, 2019 <sup>145</sup>	Serious	Moderate	Low	Low	Low	Low	Moderate
Ma, 2016 <sup>118</sup>	Serious	Moderate	Low	Moderate	Low	Low	Moderate
Mozaffarian, 2011 <sup>42</sup>	Serious	Moderate	Low	Low	Low	Serious	Moderate
Nettleton, 2009 <sup>149</sup>	Moderate	Low	Moderate	Moderate	Low	Low	Moderate
Pan, 2013 <sup>46</sup>	Serious	Moderate	Low	Low	Low	Serious	Moderate
Qi, 2012 <sup>127</sup>	Moderate	Low	Low	Low	Moderate	Moderate	Moderate
Schulze, 2004 <sup>152</sup>	Serious	Low	Low	Low	Moderate	Serious	Moderate
Stern, 2017 <sup>131</sup>	Serious	Low	Low	Low	Moderate	Serious	Moderate

<sup>lxiv</sup> A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

<sup>lxv</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)



## METHODOLOGY

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The NESR team used its rigorous, protocol-driven methodology to support the 2020 Dietary Guidelines Advisory Committee in conducting this systematic review.

NESR's systematic review methodology involves:

- Developing a protocol,
- Searching for and selecting studies,
- Extracting data from and assessing the risk of bias of each included study,
- Synthesizing the evidence,
- Developing conclusion statements,
- Grading the evidence underlying the conclusion statements, and
- Recommending future research.

A detailed description of the methodology used in conducting this systematic review is available on the NESR website: <https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews>, and can be found in the 2020 Dietary Guidelines Advisory Committee Report, Part C: Methodology.<sup>lxvi</sup> This systematic review was peer reviewed by Federal scientists, and information about the peer review process can also be found in the Committee's Report, Part C. Methodology. Additional information about this systematic review, including a description of and rationale for any modifications made to the protocol can be found in the 2020 Dietary Guidelines Advisory Committee Report, Chapter 10. Beverages.

Below are details of the final protocol for the systematic review described herein, including the:

- Analytic framework
- Literature search and screening plan
- Literature search and screening results

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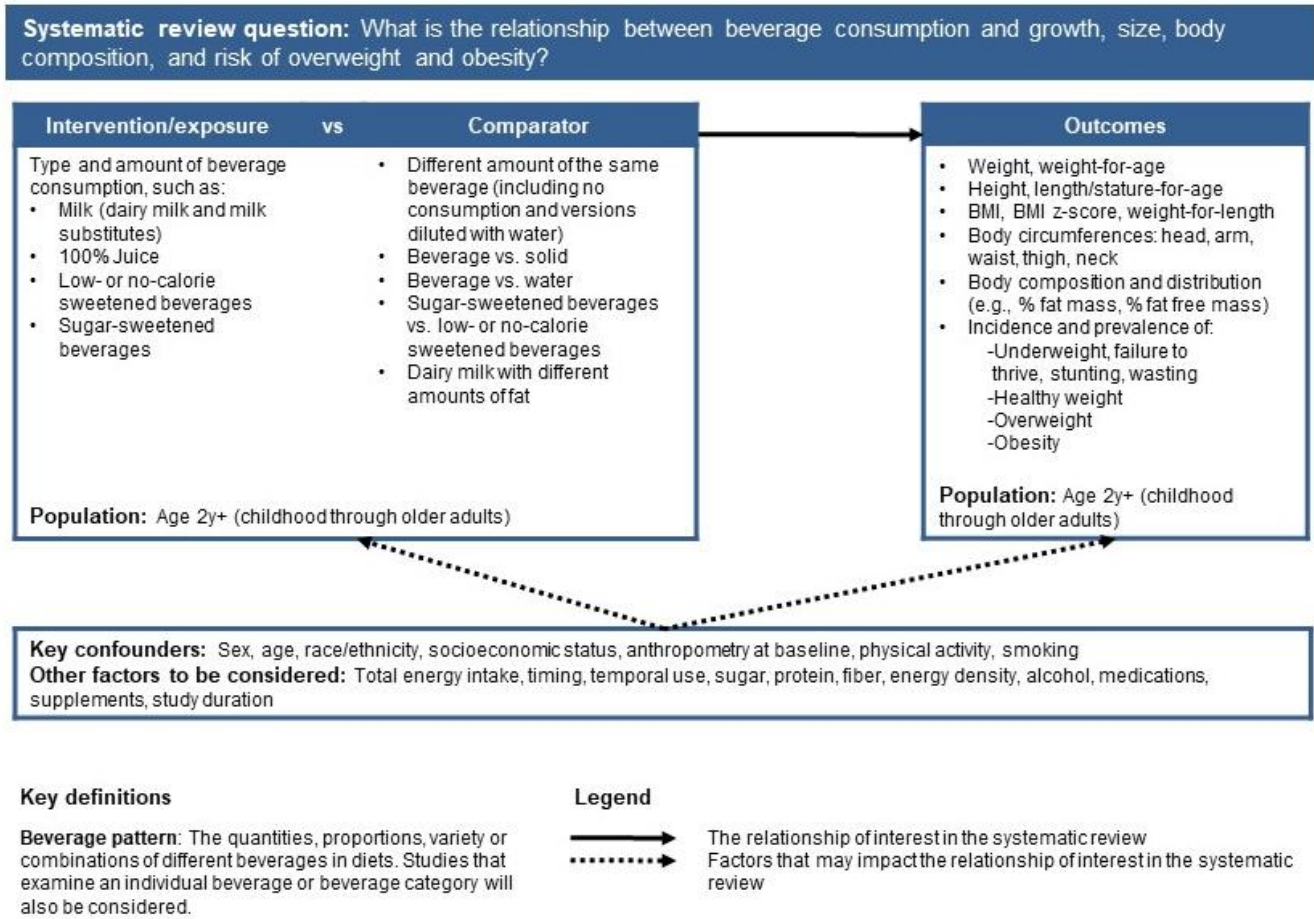
<sup>lxvi</sup> Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.



ANALYTIC FRAMEWORK

The analytic framework (Figure 1) illustrates the overall scope of the systematic review, including the population, the interventions and/or exposures, comparators, and outcomes of interest. It also includes definitions of key terms and identifies key confounders considered in the systematic review. The inclusion and exclusion criteria that follow provide additional information about how parts of the analytic framework were defined and operationalized for the review.

Figure 1. Analytic framework



## LITERATURE SEARCH AND SCREENING PLAN

### Inclusion and exclusion criteria

This table (**Table 32**) provides the inclusion and exclusion criteria for the systematic review. The inclusion and exclusion criteria are a set of characteristics used to determine which articles identified in the literature search were included in or excluded from the systematic review.

**Table 32. Inclusion and exclusion criteria**

Category	Inclusion Criteria	Exclusion Criteria
<b>Study design</b>	<ul style="list-style-type: none"> <li>• Randomized controlled trials</li> <li>• Non-randomized controlled trials (including quasi experimental and controlled before-and-after studies)</li> <li>• Prospective cohort studies</li> <li>• Retrospective cohort studies</li> <li>• Nested case-control studies</li> <li>• Mendelian randomization studies</li> </ul>	<ul style="list-style-type: none"> <li>• Uncontrolled trials</li> <li>• Case-control studies</li> <li>• Cross-sectional studies</li> <li>• Uncontrolled before-and-after studies</li> <li>• Obesity treatment studies</li> <li>• Narrative reviews</li> <li>• Systematic reviews</li> <li>• Meta-analyses</li> </ul>
<b>Intervention/exposure</b>	<p>Type and amount of beverage consumption of the following beverage types:</p> <ul style="list-style-type: none"> <li>• Milk (dairy milk and milk substitutes, including flavored milk)</li> <li>• 100% Juice</li> <li>• Low- or no-calorie sweetened beverages (LNCSB)</li> <li>• Sugar-sweetened beverages (SSB)</li> </ul>	<ul style="list-style-type: none"> <li>• Other beverage types, including: Coffee, tea, water, and nutritional beverages (e.g., protein shakes, smoothies)</li> <li>• Studies focusing on specific nutrients added to beverages instead of a beverage as a whole (i.e., studies where beverages are the delivery mechanism for a nutrient)</li> <li>• Beverages that are not commercially available (e.g., experimentally manipulated beverages)</li> <li>• Supplements</li> <li>• Alcohol</li> <li>• Soups</li> </ul>

Category	Inclusion Criteria	Exclusion Criteria
<b>Comparator</b>	<ul style="list-style-type: none"> <li>• Different amount of the same beverage (including no consumption and versions diluted with water)</li> <li>• Beverage vs. solid</li> <li>• Beverage vs. water</li> <li>• Sugar-sweetened beverages vs. low- or no-calorie sweetened beverages</li> <li>• Dairy milk with different amounts of fat</li> </ul>	<ul style="list-style-type: none"> <li>• No comparator</li> <li>• Studies comparing different types of beverages (with the exception of studies comparing a beverage to plain water, dairy milk with different amounts of fat, and sugar-sweetened beverages to low- or no-calorie sweetened beverages)</li> </ul>
<b>Outcomes</b>	<ul style="list-style-type: none"> <li>• Weight, weight-for-age</li> <li>• Height, length/stature-for-age</li> <li>• BMI, BMI z-score, weight-for-length</li> <li>• Body circumferences: head, arm, waist, thigh, neck</li> <li>• Body composition and distribution (e.g., % fat mass, % fat free mass)</li> <li>• Incidence and prevalence of: <ul style="list-style-type: none"> <li>○ Underweight, failure to thrive, stunting, wasting</li> <li>○ Healthy weight</li> <li>○ Overweight</li> <li>○ Obesity</li> </ul> </li> </ul>	
<b>Date of publication</b>	<ul style="list-style-type: none"> <li>• For Milk, Juice, LNCSB: January 2000 – June 2019</li> <li>• For SSB: January 2012 – June 2019<sup>lxvii</sup></li> </ul>	<ul style="list-style-type: none"> <li>• For Milk, Juice, LNCSB: Articles published prior to 2000</li> <li>• For SSB: articles published prior to 2012</li> </ul>
<b>Publication status</b>	<ul style="list-style-type: none"> <li>• Articles published in peer-reviewed journals</li> </ul>	<ul style="list-style-type: none"> <li>• Articles not published in peer-reviewed journals, including unpublished data, manuscripts, reports, pre-prints, abstracts, and conference proceedings</li> </ul>
<b>Language of publication</b>	<ul style="list-style-type: none"> <li>• Articles published in English</li> </ul>	<ul style="list-style-type: none"> <li>• Articles published in languages other than English</li> </ul>

<sup>lxvii</sup> This publication date range criteria was applied to the review of SSB evidence because the 2015 Dietary Guidelines Advisory Committee reviewed evidence on the relationship between added sugars, including SSB, and body weight/obesity, published up to January 2012.

Category	Inclusion Criteria	Exclusion Criteria
<b>Country<sup>lxviii</sup></b>	<ul style="list-style-type: none"> <li>Studies conducted in Very High or High Human Development Countries</li> </ul>	<ul style="list-style-type: none"> <li>Studies conducted in Medium or lower Human Development Countries</li> </ul>
<b>Study participants</b>	<ul style="list-style-type: none"> <li>Human subjects</li> <li>Males</li> <li>Females (including pregnant and lactating women)</li> </ul>	<ul style="list-style-type: none"> <li>Animal subjects</li> <li>Hospitalized samples</li> </ul>
<b>Age of study participants</b>	<ul style="list-style-type: none"> <li>Age at intervention or exposure: <ul style="list-style-type: none"> <li>Child (2-5 years)</li> <li>Child (6-12 years)</li> <li>Adolescents (13-18 years)</li> <li>Adults (19 and older)</li> <li>Older adults (65+ years)</li> </ul> </li> <li>Age at outcome: <ul style="list-style-type: none"> <li>Child (2-5 years)</li> <li>Child (6-12 years)</li> <li>Adolescents (13-18 years)</li> <li>Adults (19 and older)</li> <li>Older adults (65+ years)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Age at intervention or exposure: &lt;2y</li> <li>Age at outcome: &lt;2y</li> </ul>
<b>Health status of study participants</b>	<ul style="list-style-type: none"> <li>Studies that enroll participants who are healthy and/or at risk for chronic disease</li> <li>Studies that enroll <i>some</i> participants diagnosed with a disease</li> <li>Studies that enroll <i>some</i> participants who are classified as underweight, stunted, wasted, or obese</li> </ul>	<ul style="list-style-type: none"> <li>Studies that <i>exclusively</i> enroll participants diagnosed with a disease, or hospitalized with an illness or injury</li> <li>Studies that <i>exclusively</i> enroll participants classified as obese (i.e., studies that aim to treat participants who have already been classified as obese)</li> </ul>

<sup>lxviii</sup> The Human Development classification was based on the Human Development Index (HDI) ranking from the year the study intervention occurred or data were collected (UN Development Program. HDI 1990-2017 HDRO calculations based on data from UNDESA (2017a), UNESCO Institute for Statistics (2018), United Nations Statistics Division (2018b), World Bank (2018b), Barro and Lee (2016) and IMF (2018). Available from: <http://hdr.undp.org/en/data>). If the study did not report the year in which the intervention occurred or data were collected, the HDI classification for the year of publication was applied. HDI values are available from 1980, and then from 1990 to present. If a study was conducted prior to 1990, the HDI classification from 1990 was applied. If a study was conducted in 2018 or 2019, the most current HDI classification was applied. When a country was not included in the HDI ranking, the current country classification from the World Bank was used instead (The World Bank. World Bank country and lending groups. Available from: <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-country-and-lending-groups>).

## Electronic databases and search terms

Listed below are the databases searched to identify all potentially relevant articles that have been published to address the update to the existing systematic review.

### PubMed

- Provider: U.S. National Library of Medicine
- Date(s) Searched: June 20, 2019
- Date range searched: January 1, 2000-June 20, 2019
- Search Terms:

**#1** - "Beverages"[Mesh:NoExp] OR beverage[tiab] OR beverages[tiab] OR sports drink\* OR protein drink\* OR fortified drink\* OR sweetened drink\* OR sweet drink\* OR sugary drink\* OR dairy drink\* OR chocolate drink\* OR nutritional drink\* OR smoothie\*[tiab] OR protein shake\* OR meal replacement\*[tiab] OR carbonated drink\*[tiab] OR soft drink\*[tiab] OR soda[tiab] OR sodas[tiab] OR caffeinated drink\*[tiab] OR "Drinking Water"[Mesh] OR drinking water[tiab] OR bottled water[tiab] OR "Carbonated Beverages"[Mesh] OR carbonated water[tiab] OR sparkling water[tiab] OR flavored water[tiab] OR flavoured water[tiab] OR flavoured drink[tiab] OR flavored drink\* OR "Energy Drinks"[Mesh] OR energy drink\*[tiab] OR sugar sweetened drink\* OR "Fruit and Vegetable Juices"[Mesh] OR juice[tiab] OR juices[tiab] OR fruit drink\* OR fizzy drink\* OR "Coffee"[Mesh] OR coffee[tiab] OR "Tea"[Mesh] OR tea[tiab] OR "Milk"[Mesh:NoExp] OR milk[tiab] OR "Soy Milk"[Mesh] OR soymilk[tiab] OR "Buttermilk"[Mesh] OR buttermilk[tiab] OR "Whey"[Mesh] OR whey[tiab] OR liquid[tiab] OR liquids[tiab]

**#2** - "Body Composition"[Mesh] OR body composition[tiab] OR fat mass[tiab] OR fat free mass[tiab] OR healthy weight[tiab] OR underweight[tiab] OR wasting[tiab] OR failure to thrive[tiab] OR "Waist Circumference"[Mesh] OR waist circumference[tiab] OR head circumference[tiab] OR arm circumference[tiab] OR thigh circumference[tiab] OR neck circumference[tiab] OR "Body Height"[Mesh:NoExp] OR body height[tiab] OR stunting[tiab] OR stunted[tiab] OR "Overweight"[Mesh] OR overweight[tiab] OR obesity[tiab] OR obese[tiab] OR "Body Mass Index"[Mesh] OR body mass index[tiab] OR BMI[tiab] OR body fat[tiab]

**#3** - (#1 AND #2) NOT (("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))) NOT (editorial[ptyp] OR comment[ptyp] OR news[ptyp] OR letter[ptyp] OR review[ptyp] OR systematic review[ptyp] OR systematic review[ti] OR meta-analysis[ptyp] OR meta-analysis[ti] OR meta-analyses[ti] OR retracted publication[ptyp] OR retraction of publication[ptyp] OR retraction of publication[tiab] OR retraction notice[ti]) Filters: Publication date from 2000/01/01 to 2019/06/20; English

### Cochrane Central Register of Controlled Trials (CENTRAL)

- Provider: John Wiley & Sons
- Date(s) Searched: June 20, 2019
- Date range searched: January 1, 2000-June 20, 2019
- Search Terms:

**#1** - [mh ^Beverages] OR [mh "Drinking Water"] OR [mh "Carbonated Beverage"] OR [mh "Energy Drink"] OR [mh "Fruit and Vegetable Juice"] OR [mh Coffee] OR [mh ^Milk]

**#2** - (beverage OR beverages OR "sports drink" OR "protein drink" OR "fortified drink" OR

"sweetened drink" OR "sweet drink" OR "sugary drink" OR "dairy drink" OR "chocolate drink" OR "nutritional drink" OR smoothie\* OR "protein shake" OR "meal replacement" OR "carbonated drink" OR "soft drink" OR soda OR sodas OR "caffeinated drink" OR "drinking water" OR "bottled water" OR "carbonated water" OR "sparkling water" OR "flavored water" OR "flavoured water" OR "flavoured drink" OR "flavored drink\*" OR "energy drink" OR "sugar sweetened drink" OR juice OR juices OR "fruit drink" OR "fizzy drink" OR coffee OR tea OR milk OR soymilk OR buttermilk OR whey OR liquid OR liquids):ti,ab,kw"

**#3** - #1 OR #2"

**#4** - [mh "Body Composition"] OR [mh "Waist Circumference"] OR [mh ^"Body Height"] OR [mh "Overweight"] OR [mh "Body Mass Index"]

**#5** - ("body composition" OR "fat mass" OR "fat free mass" OR "healthy weight" OR underweight OR wasting OR "failure to thrive" OR "waist circumference" OR "head circumference" OR "arm circumference" OR "thigh circumference" OR "neck circumference" OR "body height" OR stunting OR stunted OR overweight OR obesity OR obese OR "body mass index" OR BMI OR "body fat"):ti,ab,kw"

**#6**- #4 OR #5

**#7** - #3 AND #6 with Publication Year from 2000 to 2019, in Trials (Word variations have been searched)

## Embase

- Provider: Elsevier
- Date(s) Searched: June 20, 2019
- Date range searched: January 1, 2000-June 20, 2019
- Search Terms:

**#1**- 'beverage'/mj OR 'drinking water'/mj OR 'carbonated beverage'/de OR 'energy drink'/de OR 'fruit and vegetable juice'/exp/mj OR 'coffee'/exp/mj OR 'milk'/mj OR 'soybean milk'/de OR 'buttermilk'/de OR 'whey'/de

**#2** - beverage OR beverages OR 'sports drink\*' OR 'protein drink\*' OR 'fortified drink\*' OR 'sweetened drink\*' OR 'sweet drink\*' OR 'sugary drink\*' OR 'dairy drink\*' OR 'chocolate drink\*' OR 'nutritional drink\*' OR smoothie\* OR 'protein shake\*' OR 'meal replacement\*' OR 'carbonated drink\*' OR 'soft drink\*' OR soda OR sodas OR 'caffeinated drink\*' OR 'drinking water' OR 'bottled water' OR 'carbonated water' OR 'sparkling water' OR 'flavored water' OR 'flavoured water' OR 'flavoured drink' OR 'flavored drink\*' OR 'energy drink\*' OR 'sugar sweetened drink\*' OR juice OR juices OR 'fruit drink\*' OR 'fizzy drink\*' OR coffee OR tea OR milk OR soymilk OR buttermilk OR whey OR liquid OR liquids

**#3** - #1 OR #2

**#4** - 'body composition'/exp OR 'waist circumference'/de OR 'body height'/de OR 'obesity'/exp OR 'body mass'/de

**#5** - 'body composition':ab,ti OR 'fat mass':ab,ti OR 'fat free mass':ab,ti OR 'healthy weight':ab,ti OR underweight:ab,ti OR wasting:ab,ti OR 'failure to thrive':ab,ti OR 'waist circumference':ab,ti OR 'head circumference':ab,ti OR 'arm circumference':ab,ti OR 'thigh circumference':ab,ti OR 'neck circumference':ab,ti OR 'body height':ab,ti OR stunting:ab,ti OR stunted:ab,ti OR overweight:ab,ti OR obesity:ab,ti OR obese:ab,ti OR 'body mass index':ab,ti OR bmi:ab,ti OR 'body fat':ab,ti

**#6** - #4 OR #5

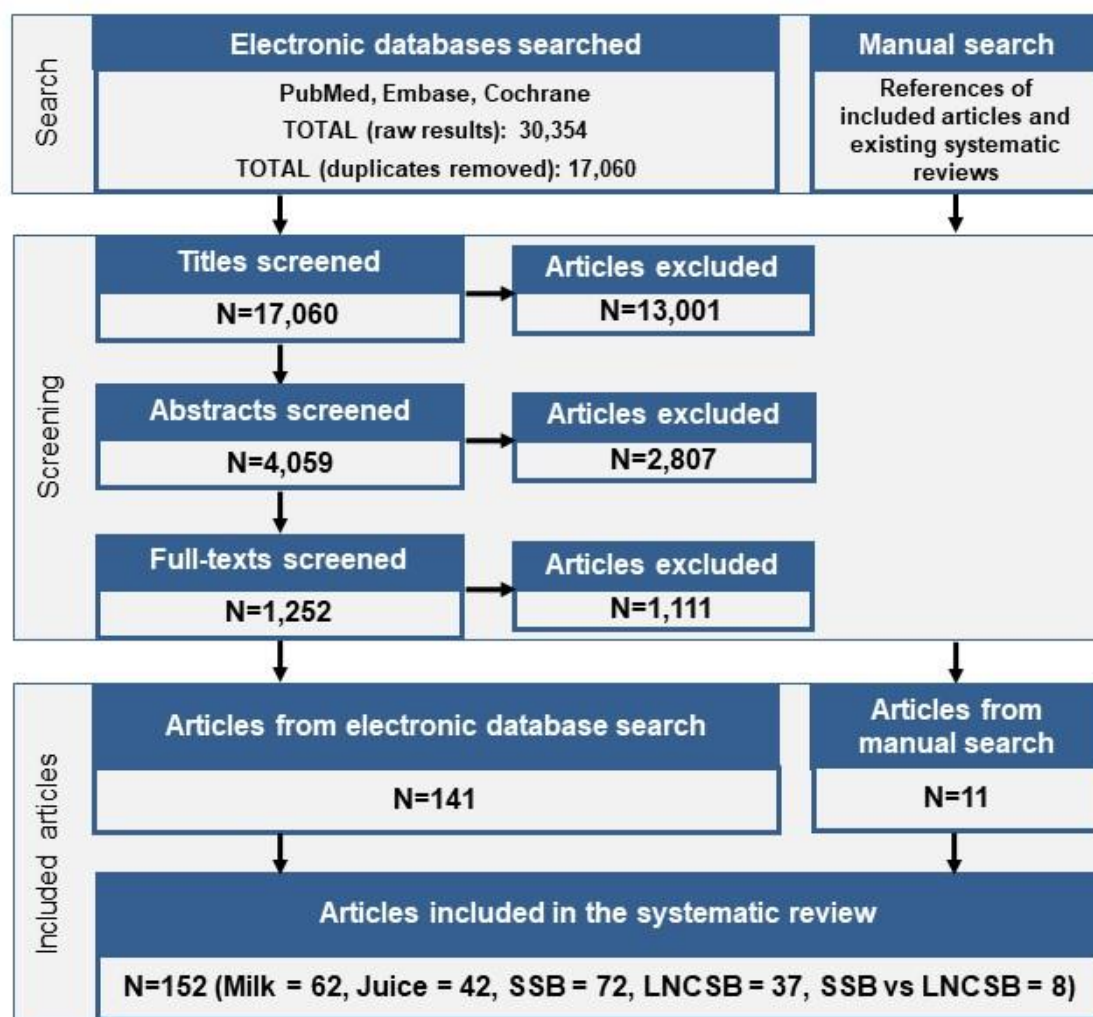
**#7** - #3 AND #6

**#8** - #3 AND #6 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim AND [english]/lim AND [2000-2019]/py NOT ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [systematic review]/lim OR [meta analysis]/lim)

## LITERATURE SEARCH AND SCREENING RESULTS

The flow chart (**Figure 2**) below illustrates the literature search and screening results for articles examining the systematic review question. The results of the electronic database searches, after removal of duplicates, were screened independently by two NESR analysts using a step-wise process by reviewing titles, abstracts, and full-texts to determine which articles met the inclusion criteria. Refer to **Table 33** for the rationale for exclusion for each excluded full-text article. A manual search was done to find articles that were not identified when searching the electronic databases; all manually identified articles are also screened to determine whether they meet criteria for inclusion.

**Figure 2. Flow chart of literature search and screening results<sup>lxix</sup>**



<sup>lxix</sup> SSB: Sugar-sweetened beverage; LNCSB: Low and no-calorie sweetened beverage



## Included articles

1. Zheng M, Allman-Farinelli M, Heitmann BL, et al. Liquid versus solid energy intake in relation to body composition among Australian children. *J Hum Nutr Diet*. 2015;28 Suppl 2:70-79. doi: 10.1111/jhn.12223.
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## Excluded articles

The table below lists the articles excluded after full-text screening, and includes columns for the categories of inclusion and exclusion criteria (see **Table 32**) that studies were excluded based on. At least one reason for exclusion is provided for each article, which may not reflect all possible reasons. Information about articles excluded after title and abstract screening is available upon request.

**Table 33. Articles excluded after full text screening with rationale for exclusion**

Citation	Rationale
<b>1</b> Adam, S, Westenhoefer, J, Rudolphi, B, Kraaibeek, HK. Three- and five-year follow-up of a combined inpatient-outpatient treatment of obese children and adolescents. <i>Int J Pediatr.</i> 2013. 2013:856743. doi:10.1155/2013/856743.	Intervention/exposure
<b>2</b> Adams, A, LaRowe, T, Cronin, KA, Prince, RJ, Jobe, JB. Healthy children, strong families: results of a randomized trial of obesity prevention for preschool American Indian children and their families. <i>Obesity (silver spring, md.).</i> 2011. 19:S110-. doi:10.1038/oby.2011.226.	Publication status
<b>3</b> Adams, A, Receveur, O, Mundt, M, Paradis, G, Macaulay, AC. Healthy lifestyle indicators in children (grades 4 to 6) from the Kahnawake Schools Diabetes Prevention Project. <i>Canadian Journal of Diabetes.</i> 2005. 29:403-409.	Study design
<b>4</b> Aeberli, I, Gerber, PA, Hochuli, M, Haile, S, Gouni-Berthold, I, Berthold, HK, Spinass, GA, Berneis, K. Low to moderate consumption of sugar-sweetened beverages impairs glucose and lipid metabolism and promotes inflammation in healthy young men - A randomized, controlled trial. <i>Obesity reviews.</i> 2011. 12:54-55. doi:10.1111/j.1467-789X.2011.00888.x.	Intervention/exposure; Comparator
<b>5</b> Afzalpour, ME, Ghasemi, E, Zarban, A. Effects of 10 weeks of high intensity interval training and green tea supplementation on serum levels of Sirtuin-1 and peroxisome proliferator-activated receptor gamma co-activator 1-alpha in overweight women. <i>Science and Sports.</i> 2017. 32:82-90. doi:10.1016/j.scispo.2016.09.004.	Intervention/exposure
<b>6</b> Agerholm-Larsen, L, Raben, A, Haulrik, N, Hansen, AS, Manders, M, Astrup, A. Effect of 8 week intake of probiotic milk products on risk factors for cardiovascular diseases. <i>Eur J Clin Nutr.</i> 2000. 54:288-97.	Intervention/exposure
<b>7</b> Agin, D, Kotler, DP, Papandreou, D, Liss, M, Wang, J, Thornton, J, Gallagher, D, Pierson, RN, Jr. Effects of whey protein and resistance exercise on body composition and muscle strength in women with HIV infection. <i>Ann N Y Acad Sci.</i> 2000. 904:607-9. doi:10.1111/j.1749-6632.2000.tb06523.x.	Health status
<b>8</b> Agudelo-Ochoa, GM, Pulgarin-Zapata, IC, Velasquez-Rodriguez, CM, Duque-Ramirez, M, Naranjo-Cano, M, Quintero-Ortiz, MM, Lara-Guzman, OJ, Munoz-Durango, K. Coffee Consumption Increases the Antioxidant Capacity of Plasma and Has No Effect on the Lipid Profile or Vascular Function in Healthy Adults in a Randomized Controlled Trial. <i>J Nutr.</i> 2016. 146:524-31. doi:10.3945/jn.115.224774.	Outcome
<b>9</b> Ahmad, R, Mok, A, Rangan, AM, Louie, JCY. Association of free sugar intake with blood pressure and obesity measures in Australian adults. <i>Eur J Nutr.</i> 2019. doi:10.1007/s00394-019-01932-7.	Study design
<b>10</b> Aiso, I, Inoue, H, Seiyama, Y, Kuwano, T. Compared with the intake of commercial vegetable juice, the intake of fresh fruit and komatsuna ( <i>Brassica rapa</i> L. var. <i>perviridis</i> ) juice mixture reduces serum cholesterol in middle-aged men: a randomized controlled pilot study. <i>Lipids Health Dis.</i> 2014. 13:102. doi:10.1186/1476-511x-13-102.	Comparator

Citation	Rationale
11 Aizawa, T, Yamamoto, A, Ueno, T. Effect of oral theaflavin administration on body weight, fat, and muscle in healthy subjects: a randomized pilot study. <i>Biosci Biotechnol Biochem.</i> 2017. 81:311-315. doi:10.1080/09168451.2016.1246170.	Intervention/exposure
12 Akazome, Y, Kametani, N, Kanda, T, Shimasaki, H, Kobayashi, S. Evaluation of safety of excessive intake and efficacy of long-term intake of beverages containing apple polyphenols. <i>J Oleo Sci.</i> 2010. 59:321-38.	Comparator
13 Akazome, Y, Kanda, T, Ohtake, Y, Hashimoto, H, Kametani, N, Sato, K, Nakamura, T, Kajimoto, Y. Evaluation of safety of excessive intake and efficacy of long term intake of beverage containing polyphenols derived from apples. <i>Japanese pharmacology and therapeutics.</i> 2005. 33:893-911.	Language
14 Albala, C, Ebbeling, CB, Cifuentes, M, Lera, L, Bustos, N, Ludwig, DS. Effects of replacing the habitual consumption of sugar-sweetened beverages with milk in Chilean children. <i>Am J Clin Nutr.</i> 2008. 88:605-11. doi:10.1093/ajcn/88.3.605.	Intervention/exposure
15 Alderete, E, Bejarano, I, Rodriguez, A. Beverage intake and obesity in early childhood: evidence form primary health care clients in Northwest Argentina. <i>J Dev Orig Health Dis.</i> 2016. 7:244-252. doi:10.1017/s204017441500793x.	Study design
16 Aldrich, ND, Reicks, MM, Sibley, SD, Redmon, JB, Thomas, W, Raatz, SK. Varying protein source and quantity do not significantly improve weight loss, fat loss, or satiety in reduced energy diets among midlife adults. <i>Nutr Res.</i> 2011. 31:104-12. doi:10.1016/j.nutres.2011.01.004.	Intervention/exposure
17 Alexy, U, Reinehr, T, Sichert-Hellert, W, Wollenhaupt, A, Kersting, M, Andler, W. Positive changes of dietary habits after an outpatient training program for overweight children. <i>Nutrition Research.</i> 2006. 26:202-208. doi:10.1016/j.nutres.2006.05.007.	Intervention/exposure
18 Al-Haggar, M, Yahia, N, Ghanem, H. High dairy calcium intake in pubertal girls: Relation to weight gain and bone mineral status. <i>Journal of Medical Sciences.</i> 2006. 6:631-635.	Intervention/exposure
19 Alhamhany, NN, Alassady, EH. Does green coffee has a positive effect on body mass index and lipid profile in a sample of obese people. <i>Journal of Pharmaceutical Sciences and Research.</i> 2018. 10:627-630.	Intervention/exposure; Country
20 Ali, A, Yazaki, Y, Njike, VY, Ma, Y, Katz, DL. Effect of fruit and vegetable concentrates on endothelial function in metabolic syndrome: A randomized controlled trial. <i>Nutrition Journal.</i> 2011. 10. doi:10.1186/1475-2891-10-72.	Intervention/exposure
21 Allison, DB, Gadbury, G, Schwartz, LG, Murugesan, R, Kraker, JL, Heshka, S, Fontaine, KR, Heymsfield, SB. A novel soy-based meal replacement formula for weight loss among obese individuals: a randomized controlled clinical trial. <i>Eur J Clin Nutr.</i> 2003. 57:514-22. doi:10.1038/sj.ejcn.1601587.	Intervention/exposure
22 Al-Naggar, RA, Osman, MT, Abdulghani, M. Effects green tea on the body weight of malaysian young obese females: Single blinded clinical trail study. <i>Research Journal of Pharmaceutical, Biological and Chemical Sciences.</i> 2013. 4:1649-1655.	Intervention/exposure
23 Alonso, A, Zozaya, C, Vazquez, Z, Alfredo Martinez, J, Martinez-Gonzalez, MA. The effect of low-fat versus whole-fat dairy product intake on blood pressure and weight in young normotensive adults. <i>J Hum Nutr Diet.</i> 2009. 22:336-42. doi:10.1111/j.1365-277X.2009.00967.x.	Intervention/exposure
24 Alperet, DJ, Rebello, SA, Khoo, Ey-H, Tay, Z, Seah, Ss-Y, Tai, BC, Tai, ES, Emady-Azar, S, Chou, CJ, Darimont, C, et al, . The effects of coffee consumption on insulin sensitivity and other risk factors for type 2 diabetes. <i>Circulation.</i> 2018. 137.	Publication status

Citation	Rationale
<b>25</b> Alves, NE, Enes, BN, Martino, HS, Alfenas Rde, C, Ribeiro, SM. Meal replacement based on Human Ration modulates metabolic risk factors during body weight loss: a randomized controlled trial. <i>Eur J Nutr.</i> 2014. 53:939-50. doi:10.1007/s00394-013-0598-3.	Intervention/exposure; Comparator
<b>26</b> Amagase, H, Nance, DM. A randomized, double-blind, placebo-controlled, clinical study of the general effects of a standardized <i>Lycium barbarum</i> (Goji) Juice, GoChi. <i>J Altern Complement Med.</i> 2008. 14:403-12. doi:10.1089/acm.2008.0004.	Intervention/exposure; Comparator
<b>27</b> Amagase, H, Nance, DM. A randomized, double-blind, placebo-controlled, clinical study of the general effects of a standardized <i>Lycium barbarum</i> (goji) juice, GoChi™. <i>Journal of Alternative and Complementary Medicine.</i> 2008. 14:403-412. doi:10.1089/acm.2008.0004.	Comparator; Duplicate
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<b>552</b> Lee, R. Beverages: The Good, the Bad and the Ugly. <i>Explore: The Journal of Science and Healing.</i> 2008. 4:210-212. doi:10.1016/j.explore.2008.02.012.	Study design
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<b>554</b> Lee, SM, Kim, S, Lim, CG. The effects of milk intake and whole-body vibration exercise on bone mineral density in elderly women in nursing homes. <i>J Phys Ther Sci.</i> 2017. 29:1125-1128. doi:10.1589/jpts.29.1125.	Intervention/exposure
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<b>560</b> Levy, Y, Narotzki, B, Reznick, AZ. Green tea, weight loss and physical activity. <i>Clinical nutrition (edinburgh, scotland).</i> 2017. 36:315. doi:10.1016/j.clnu.2016.11.001.	Study design
<b>561</b> Li, J, Wang, Y. Tracking of dietary intake patterns is associated with baseline characteristics of urban low-income African-American adolescents. <i>J Nutr.</i> 2008. 138:94-100. doi:10.1093/jn/138.1.94.	Outcome
<b>562</b> Li, S, Guerin-Deremau, L, Pochat, M, Wils, D, Reifer, C, Miller, LE. NUTRIOSE dietary fiber supplementation improves insulin resistance and determinants of metabolic syndrome in overweight men: a double-blind, randomized, placebo-controlled study. <i>Appl Physiol Nutr Metab.</i> 2010. 35:773-82. doi:10.1139/h10-074.	Intervention/exposure; Country
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<b>705</b> Mueller, NT, Odegaard, AO, Gross, MD, Koh, WP, Yu, MC, Yuan, JM, Pereira, MA. Soy intake and risk of type 2 diabetes mellitus in Chinese Singaporeans: Soy intake and risk of type 2 diabetes. <i>European Journal of Nutrition</i> . 2012. 51:1033-1040. doi:10.1007/s00394-011-0276-2.	Outcome
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<b>710</b> Mytton, OT, Eyles, H, Ogilvie, D. Evaluating the Health Impacts of Food and Beverage Taxes. <i>Curr Obes Rep</i> . 2014. 3:432-9. doi:10.1007/s13679-014-0123-x.	Intervention/exposure
<b>711</b> Nabi, BN, Sedighinejad, A, Haghighi, M, Farzi, F, Rimaz, S, Atrkarroushan, Z, Biazar, G. The anti-obesity effects of green tea: A controlled, randomized, clinical trial. <i>Iranian Red Crescent Medical Journal</i> . 2018. 20. doi:10.5812/ircmj.55950.	Intervention/exposure
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<b>787</b> Phelan, S, Wing, RR, Brannen, A, McHugh, A, Hagobian, T, Schaffner, A, Jelalian, E, Hart, CN, Scholl, TO, Munoz-Christian, K, Yin, E, Phipps, MG, Keadle, S, Abrams, B. Does Partial Meal Replacement During Pregnancy Reduce 12-Month Postpartum Weight Retention?. <i>Obesity (Silver Spring).</i> 2019. 27:226-236. doi:10.1002/oby.22361.	Intervention/exposure
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<b>862</b> Santiago-Torres, M, Cui, Y, Adams, AK, Allen, DB, Carrel, AL, Guo, JY, Delgado-Rendon, A, LaRowe, TL, Schoeller, DA. Familial and individual predictors of obesity and insulin resistance in urban Hispanic children. <i>Pediatr Obes</i> . 2016. 11:54-60. doi:10.1111/ijpo.12020.	Study design
<b>863</b> Santiago-Torres, M, Cui, Y, Adams, AK, Allen, DB, Carrel, AL, Guo, JY, LaRowe, TL, Schoeller, DA. Structural equation modeling of the associations between the home environment and obesity-related cardiovascular fitness and insulin resistance among Hispanic children. <i>Appetite</i> . 2016. 101:23-30. doi:10.1016/j.appet.2016.02.003.	Study design
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<b>929</b> Steurer, J. Drinking water before eating promotes weight loss. <i>Praxis.</i> 2016. 105:107-108. doi:10.1024/1661-8157/a002254.	Language
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<b>932</b> St-Onge, MP, Salinardi, T, Herron-Rubin, K, Black, RM. A weight-loss diet including coffee-derived manooligosaccharides enhances adipose tissue loss in overweight men but not women. <i>Obesity (Silver Spring).</i> 2012. 20:343-8. doi:10.1038/oby.2011.289.	Intervention/exposure
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<b>934</b> Stookey, JD, Constant, F, Popkin, BM, Gardner, CD. Drinking water is associated with weight loss in overweight dieting women independent of diet and activity. <i>Obesity (Silver Spring).</i> 2008. 16:2481-8. doi:10.1038/oby.2008.409.	Intervention/exposure
<b>935</b> Stookey, JD, Del Toro, R, Hamer, J, Medina, A, Higa, A, Ng, V, TinajeroDeck, L, Juarez, L. Qualitative and/or quantitative drinking water recommendations for pediatric obesity treatment. <i>J Obes Weight Loss Ther.</i> 2014. 4:232. doi:10.4172/2165-7904.1000232.	Intervention/exposure; Comparator
<b>936</b> Strand, MA, Perry, J, Wang, P, Liu, S, Lynn, H. Risk factors for metabolic syndrome in a cohort study in a north China urban middle-aged population. <i>Asia Pac J Public Health.</i> 2015. 27:Np255-65. doi:10.1177/1010539512438609.	Study design; Outcome
<b>937</b> Suder, A, Janusz, M, Jagielski, P, Glodzik, J, Palka, T, Cison, T, Pilch, W. Prevalence and risk factors of abdominal obesity in Polish rural children. <i>Homo.</i> 2015. 66:357-68. doi:10.1016/j.jchb.2014.09.008.	Study design
<b>938</b> Sugihara Junior, P, Ribeiro, AS, Nabuco, HCG, Fernandes, RR, Tomeleri, CM, Cunha, PM, Venturini, D, Barbosa, DS, Schoenfeld, BJ, Cyrino, ES. Effects of Whey Protein Supplementation Associated With Resistance Training on Muscular Strength, Hypertrophy, and Muscle Quality in Preconditioned Older Women. <i>Int J Sport Nutr Exerc Metab.</i> 2018. 28:528-535. doi:10.1123/ijsnem.2017-0253.	Intervention/exposure
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<b>1077</b> Wright, LS, Rifas-Shiman, SL, Oken, E, Litonjua, AA, Gold, DR. Prenatal and Early Life Fructose, Fructose-Containing Beverages, and Midchildhood Asthma. <i>Ann Am Thorac Soc.</i> 2018. 15:217-224. doi:10.1513/AnnalsATS.201707-530OC.	Outcome
<b>1078</b> Wrotniak, BH, Georger, L, Hill, DL, Zemel, BS, Stettler, N. Association of dairy intake with weight change in adolescents undergoing obesity treatment. <i>J Public Health (Oxf).</i> 2018. . doi:10.1093/pubmed/fdy064.	Study design; Health status
<b>1079</b> Wuenstel, JW, Wadolowska, L, Slowinska, MA, Niedzwiedzka, E, Kowalkowska, J, Kurp, L. Intake of Dietary Fibre and Its Sources Related to Adolescents' Age and Gender, but Not to Their Weight. <i>Cent Eur J Public Health.</i> 2016. 24:211-216. doi:10.21101/cejph.a4331.	Study design
<b>1080</b> Xanthopoulos, MS, Moore, RH, Wadden, TA, Bishop-Gilyard, CT, Gehrman, CA, Berkowitz, RI. The association between weight loss in caregivers and adolescents in a treatment trial of adolescents with obesity. <i>J Pediatr Psychol.</i> 2013. 38:766-74. doi:10.1093/jpepsy/jst024.	Intervention/exposure; Other (e.g., duplicative data)
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<b>1085</b> Yang, H, Kim, H, Kim, JM, Chung, HW, Chang, N. Associations of dietary intake and metabolic syndrome risk parameters in Vietnamese female marriage immigrants in South Korea: The KoGES follow-up study. <i>Nutr Res Pract.</i> 2016. 10:313-20. doi:10.4162/nrp.2016.10.3.313.	Intervention/exposure; Outcome
<b>1086</b> Yang, HY, Yang, SC, Chao, JC, Chen, JR. Beneficial effects of catechin-rich green tea and inulin on the body composition of overweight adults. <i>Br J Nutr.</i> 2012. 107:749-54. doi:10.1017/s0007114511005095.	Comparator
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